RC
952
N2773
1993

National Institute on Aging. Epidemiology, Demography, and Biometry Program

Intramural annual report
1993

10/5/93

EPIDEMIOLOGY, DEMOGRAPHY, AND BIOMETRY PROGRAM
NATIONAL INSTITUTE ON AGING

INTRAMURAL ANNUAL REPORT 1993

NATIONAL INSTITUTES OF HEALTH
NIH LIBRARY
JAN 03 1994
BETHESDA, MD 20892

U.S.
DEPARTMENT
OF
HEALTH
AND
HUMAN
SERVICES

Public
Health
Service

National
Institutes
of
Health

KC
952
N2993
1993

Fiscal Year 1993

Annual Report of the Epidemiology, Demography, and Biometry Program

National Institute on Aging

ANNUAL REPORT
OF THE
EPIDEMIOLOGY, DEMOGRAPHY, AND BIOMETRY PROGRAM
NATIONAL INSTITUTE ON AGING

Overview

Mission: The Epidemiology, Demography, and Biometry Program (EDBP) (1) plans, conducts, and directs epidemiology, demography, and biometry programs relevant to the mission of the NIA; (2) collects and analyzes data regarding the distribution of the aged by such categories as sex, race, socioeconomic and demographic characteristics and serves as a focal point for these data; (3) plans, initiates, coordinates, and analyzes national and international epidemiologic longitudinal studies and studies of special populations; (4) in collaboration with NIA staff and that of other Institutes, federal agencies and scientific organizations, recommends priorities and develops epidemiologic studies of specific diseases and conditions affecting the aged; (5) provides consultation and service to NIH program areas and private organizations on epidemiology, demography, and biometry studies on aging; (6) recommends mechanisms to be used or develops mechanisms to accomplish Program objectives; (7) plans and directs research and training in the areas of epidemiology, demography, and biometry, and serves as the primary federal source of information regarding research and training in these areas.

Introduction: The EDBP, a component of the NIA intramural research program, based in Bethesda, Maryland, functions similarly to other NIH intramural programs. EDBP investigators identify hypotheses, initiate research studies, and report results in the scientific literature. EDBP "laboratories" are communities and populations often supported through competitive contracts to academic and community institutions. The Program has four units: the Epidemiology and Demography Office, the Asia-Pacific Office, the Geriatric Epidemiology Office, and the Biometry Office.

Activities consistent with the above mission statement are proceeding in a number of areas and are summarized below and in the individual Office reports.

Productivity: Highlights of published or in-press reports by EDBP staff are included with the Office reports but selected findings, most from the Established Populations for Epidemiologic Studies of the Elderly (EPESE) project, which involves longitudinal follow-up of communities, are summarized:

- The occurrence in the EPESE project of loss of mobility was predicted by various risk factors and diseases. A new heart attack, stroke, cancer or hip fracture was associated with substantially greater risk than was associated with the presence of these conditions at baseline, as was current smoking, not consuming alcohol, high body mass index, and low physical activity.

- At the age of 65, those with 12 or more years of education had an active life expectancy that was 2.4 to 3.9 years longer than those with less education, and with adjustment for education, active life expectancy was similar between blacks and whites.

- After adjustment for related factors, increased risk of pneumonia mortality was found for those with limitations in activities of daily living and cognitive impairment in both men and women.

- Septicemia mortality was associated with age, male gender, history of diabetes, smoking, disability in activities of daily living and cognitive impairment.

- A high level of recreational physical activity in the physically capable subset of the EPESE reduced the likelihood of mortality after both 3 and 6 years.

- Low education and occupation are significant predictors of development of cognitive impairment in the EPESE.

- Using data from follow-up of a national sample of white women aged 65-74 years, those with a high maximal lifetime body mass index experienced an increased risk of coronary heart disease. The relationship was enhanced when recent weight loss was accounted for in the analysis. In related analysis, lean women with stable weight had the lowest risk of all-cause mortality, while those who had lost weight have a high risk irrespective of weight.

Study Development: When the Program began approximately 15 years ago, descriptive data on aging and age-related diseases were lacking or concentrated in studies of a single disease, e.g., coronary heart disease or diabetes. Three community studies (EPESE) were created to fill the information gap, and they have provided much new and important data on health status in older persons. For example, a new estimate of Alzheimer's disease frequency was reported from the East Boston, Massachusetts population.

More recently, as a result of careful review and planning, data collection in these first-generation studies is now being completed; and direct contract support is being phased out. However, a study at one of the sites, focusing on black-white differences among elderly living in the Piedmont area of North Carolina will continue for 4 years. These studies have provided much useful data, which are yielding a great many valuable reports that are now being published by EDBP staff and collaborating scientists.

Based on hypotheses and data needs that cannot be addressed by these studies, a second-generation of studies has been developed. These were built on the expertise and research interests of EDBP staff and with outside consultation. Specifically, three new studies are completing an initial data collection phase. They are: the Women's Health and Aging Study, which is a study with a strong biomedical emphasis of the causes and course of disability in older community-dwelling women; the Honolulu Dementia and Aging study, an

addition to a long-term study of Japanese-American men in the Honolulu Heart Program that emphasizes potential risk factors for Alzheimer's disease and vascular dementia; and the Comorbidity and Cancer in the Elderly study, a collaboration with the National Cancer Institute and its large cancer registry program. Also, there has been an add-on of immunologic measures to the ongoing study in the biracial EPESE community in North Carolina and the addition of metabolic, immunologic factors, and body composition studies to the long-term heart disease study in Framingham, Massachusetts. Finally, review is proceeding on proposals resulting from an RFP for a study of the potential effect of head trauma and unconsciousness during the Second World War on the onset of Alzheimer's disease.

Proposed Studies: Efforts have been made by the EDBP leadership to incorporate biomedical issues into current and potential future EDBP research studies, and in particular to emphasize the interaction of multiple diseases (comorbidity) and the aging processes in the development of study proposals for third-generation investigations. For example, outside peer review for concept clearance and internal Contract's Advisory Committee review with recommendation to the NIA Director have been obtained for three new proposed studies:

- To enhance studies in long-lived population participating in the Honolulu Dementia and Aging Study by biomarker assessment of Apo-E status; by magnetic resonance imaging of the brain for all individuals who are either incident cases of dementia or who have an Apo-E 4 phenotype; by measuring body composition and assessing dietary habits on those long-lived persons who have different patterns of lifelong weight change.

- The Health ABC, a study of early decline in function related to change in body composition and decline in health status, targeting disease and metabolic relationships in healthier older whites and African-Americans. A vitality component may be added.

- To study the influence of age on the choice of cancer treatment made by physicians for their elderly patients. Information is being collected on cancer and comorbidity, and there are already plans to obtain data on illness behavior and quality of life from cancer patients.

Staff Development and Training Functions: Over the years the core staff have been built up through recruitment of productive trainees and external subject matter specialists. Trainees through the NIH Intramural Research Training Award Program and the USPHS Epidemiology Training Program have worked in EDBP. The latter program usually involves 1 year at a school of public health and 2 years with the Program. Currently two individuals Dr. Lori Brown, formerly of a Stanford University immunology lab and Dr. John Sorkin, a Senior Staff Fellow at the GRC, are in this epidemiology training program. Also, the rich experience and talents of foreign scientists have been utilized by the Program. Drs. Marco Pahor and Antonio Sgadari from Rome spent 3 months with the Program, and Dr. Chiara Corti has joined us for a year or more as a Visiting Fellow after one year of training in epidemiology at Johns Hopkins.

We have recruited Dr. Jean Langlois, an experienced injury studies investigator, as well as a general epidemiologist with background in speech pathology. Efforts are proceeding to fill a long vacant biostatistician position. A well trained statistician will help immensely in developing more appropriate statistical methods and sustaining the in-house capacity necessary for supporting active epidemiologic research.

Consulting and Interagency Cooperation: The intramural program has the potential for interrelationships with other institutes, government agencies, and the extramural community. A number of these collegial arrangements are detailed in the Office reports. As a representative example, the addition of a dementia component to the Honolulu Heart Program is being accomplished through an intraagency agreement with the originating institute. However, the impact of the study is being potentiated by intramural collaboration with other governmental and extramural groups. Comparison with Japanese studies is made possible through long-term Department of Energy sponsored studies. Grant supported research, including an administrative supplement, has allowed cross-national comparisons with Seattle, Washington. Workshops on various topics, such as the use of objective performance measures of functioning, immunologic indicators of aging, and cancer in the elderly have been convened as another way to promote interchange with the community.

Epidemiologic Directions: There is a continuing process of development and reappraisal of research directions of the Program by staff and outside groups. Previously, an ad hoc scientific advisory committee met regularly and provided oversight for the Program. As a result of their advice, there has been a definite recent emphasis on the identification, where possible, of biologic mechanisms as they relate to key aging issues being addressed by ongoing and planned epidemiologic studies. A complementarity of purpose exists between the EDBP and the larger NIA Intramural Research Program (IRP). The rationale for such linkage is consistent with observations made by Dr. Lilienfeld, a major contributor to the development of modern epidemiology. He has listed three general ways that information from epidemiologic studies can be used: "(1) To elucidate the etiology of a specific disease or group of diseases by combining epidemiologic data with information from other disciplines such as genetics, biochemistry and microbiology; (2) To evaluate the consistency of epidemiologic data with etiologic hypotheses developed either clinically (at the bedside) or experimentally (in the laboratory) (3) To provide the basis for developing and evaluating preventive procedures and public health practices." It is the public health potential that requires large and sometimes costly community and population-based studies dealing with aging and age-related diseases and that differentiates EDBP somewhat from the IRP. The goal of such studies is to generate sufficient population-based knowledge to make changes that would move the entire population of older persons to a more advantageous and beneficial location on the risk spectrum. These are the types of studies that EDBP staff need to continue developing, completing, and reporting on now and in the future.

Specific Activities of the Associate Director

Dr. Richard Havlik, Associate Director, EDBP is a member and Chairperson of the PHS Epidemiology Training Program Steering Committee; a member of the NIH Epidemiology Coordinating Committee, and the Biomedical Scientific Research Service Credentialing Committee. Dr. Havlik is the NIH representative to the National Death Index Advisory Committee. He gave presentations on "Comorbidity and Disability in Older-Aged Persons" to the Trieste Workshop on Cancer in the Elderly; and "Epidemiology of Hypertension: Relationship to Glucose Intolerance" to a Consensus Development Conference on Treatment of Hypertension in Diabetes organized by the American Diabetes Association. He will present in September 1993 at the annual meeting of the International Association of Cancer Registries meeting in Bratislava, Slovak Republic. He collaborated with NIA staff members on a chapter entitled "Epidemiology and Treatment of Hypertension in Older Persons" for Hypertension: Pathophysiology, Diagnosis and Management; "Epidemiology and Demography" for the Merck Manual of Geriatrics; and an editorial on " Epidemiology of Aging" for the Annals of Epidemiology.

Cancer in the Aged Subprogram

The NIA Epidemiology, Demography, and Biometry (EDB) Program began several research projects to address the cancer/aging interface in 1991. We conduct these studies in collaboration with colleagues in the National Cancer Institute (NCI).

Cancer is a leading cause of morbidity and mortality in the United States for all age groups, but it is a special problem for persons 65 years and older. Over 55 percent of all cancers occur in this subset of the population; 67 percent of cancer mortality is in this age group. In the U.S. the major tumors affecting older-aged persons are breast, prostate, colon, rectum, lung, urinary bladder, pancreas, and stomach. Only recently have these facts become recognized. Therefore, the management of cancer in older-aged patients has not been studied to any large extent. Since older cancer patients have health care needs independent of and associated with their cancer diagnosis, EDB projects address the information gaps on cancer in the elderly, especially those concerning comorbid conditions present at initial diagnosis of cancer, multiple tumors, illness behavior, and quality of life issues in surviving cancer.

EDB and the NCI Surveillance, Epidemiology, and End Results (SEER) Program have instigated development of cross-national projects that utilize the strength of selected tumor registries in Italy, the Netherlands, and the Slovak Republic to address several of these topics. Comparative international studies can provide many useful answers to questions of etiology, early detection, treatment, and the influence of aging on cancer patient management.

NIA/NCI COLLABORATIVE STUDY: COMORBIDITY AND EARLY DIAGNOSIS OF CANCER IN THE ELDERLY

The NIA and the NCI are conducting a study on cancer in the elderly using resources of the NIA EDB Program and the NCI SEER Program. Seven cancers have been designated for the NIA/NCI SEER Collaborative Study -- colon, stomach, urinary bladder, prostate, breast, ovary, and cervix uteri tumors. Study objectives are to:

- **Develop descriptive information** in response to the basic questions of what are the predominant comorbid conditions and functional limitations that exist in older-aged persons diagnosed with cancer; and what do older-aged persons do when they become aware of themselves as having cancer-suspicious signs and symptoms.

- **Develop a profile of comorbidity** and ascertain the extent to which competing health problems influence treatment of older persons diagnosed with cancer.

- **Assess illness behavior** in the elderly as a precursor to taking action for cancer signs and symptoms.

- **Generate information for application of research** into practice, promote studies on clinical interventions, and hypothesis testing to more effectively address the unique problems of cancer in aged persons (i.e., minimize morbidity, prevent loss of function, promote quality of life in parallel with appropriate medical and surgical treatment).

The major questions are: (1) do older-aged persons receive the same type of initial treatment procedures as younger persons for the same cancer sites (controlling for disease stage); (2) to what extent are concomitant disease and/or illnesses and the normal processes of aging associated with cancer treatment in older-aged persons; and (3) are older-aged persons more likely to present with advanced stages of cancer at initial diagnosis; and (4) what factors increase the length of time from recognition of symptoms to the time of diagnosis so that they are more likely to be seen in later stage disease.

The NIA/NCI SEER Collaborative Study is an "add-on" to the routine operation of six of the nine SEER Program participants -- the states of Iowa, Utah, and New Mexico, and the reporting regions of Seattle, Washington, San Francisco-Oakland, California, and Atlanta, Georgia. SEER cancer registry participants in designated U.S. geographic areas abstract information on incident cancers from hospitals in their designated regions. The large scale population-based SEER data system covers about 10 percent of the U.S. population and includes the states of Connecticut, Hawaii, and Detroit, Michigan in addition to those mentioned above. Principal investigators are responsible for consolidating all data concerning an individual cancer case and assuring quality control procedures.

The study's pilot phase (on 1712 patient records) was completed in November 1992. The pilot study established study procedures, verified efficacy of data collection forms, and created the study infrastructure to obtain information on comorbidity from medical records of cancer patients. Other information derived from the pilot study on comorbidities present, disease symptomatology, and medications at admission to the hospital provided the foundation for the full field operation (April 1993). Data will be obtained on a random sample of 7800 cancer patients with an age emphasis on those 65 years and older. A control group of patients aged 55-64 years is included. The field operation, Phase II, is scheduled for April 1, 1993 through March 31, 1994.

Instruments for the illness behavior pilot study, Phase III, will be pre-tested in late summer, early fall, 1993. The interview component of the NIA/NCI SEER Collaborative Study is scheduled to begin in early 1994; however, additional funding for this phase will need to be identified.

The NIA project officers for the NIA/NCI SEER Collaborative Study are Drs. Rosemary Yancik and Richard Havlik. NCI project officer is Dr. Brenda Edwards, Surveillance Program, Division of Cancer Prevention and Control.

IOWA EPESE/SEER STUDY ON CANCER IN THE ELDERLY

The cancer experience of 737 Iowa EPESE respondents is being investigated by Drs. Rosemary Yancik and Richard Havlik, other EDBP staff, and Dr. Jon Lemke, University of Iowa. The Iowa data from the National Cancer Institute (NCI) Surveillance, Epidemiology, and End Results (SEER) Program, a population-based national tumor registry were merged with data from the Iowa EPESE study participants. Development of the Iowa EPESE/SEER database was completed in 1992. The SEER data augment the subgroup of EPESE participants diagnosed with cancer providing the following information: (1) extent of disease at initial diagnosis (e.g., stage of the malignancy); (2) natural history of the tumor; (3) initial treatment; and (4) details on survival over time. Information is available to respond to the following questions:

Characterization of the IOWA/SEER cancer survivor cohort

1. What was the extent of each malignancy for the EPESE cancer patient/survivor at initial diagnosis (i.e., disease stage) according to specific cancer site in the baseline group?

2. What is the extent of the malignancy for the EPESE cancer patient/survivor group who developed cancer subsequent to the baseline interview? What predisposing factors can be distinguished for this group (e.g., symptoms)?

3. What chronic conditions are likely to be found in older persons with cancer? Were these present at initial diagnosis of the tumor?

4. On what social and health behavioral dimensions do persons with cancer and multiple comorbid conditions differ from those who have cancer as a single condition?

Cancer patient/survivors compared with those afflicted with other chronic diseases

5. What is the self-perceived health status of the cancer only patient/survivor group as compared with cancer and other chronic conditions patient/survivor group? How does this compare with the self-perceived health status of those not afflicted, controlling for cancer site and age?

6. Do the number and severity of the chronic conditions associated with cancer differ for those EPESE participants with heart disease?

7. Does the functional status of EPESE participants who have had a diagnosis of cancer differ from other participants diagnosed with other chronic diseases or those without a chronic disease.

8. What coping mechanisms or resources are used by cancer patients/survivors as compared with patients/survivors of other chronic diseases?

9. What deleterious behavioral factors (e.g., smoking) are associated with the complex of comorbidity and cancer.

10. What is the impact of cancer on the social functioning of older-aged persons as compared with those who have not been afflicted?

FOLLOW-UP: NIA/NCI/FOGARTY CENTER CENTRAL AND EAST EUROPEAN INITIATIVE

In 1991, with support from the National Institutes of Health (NIH) Fogarty International Center (FIC) Central and Eastern European Initiative (CEEI) and their respective Institutes, an NIA/NCI study team examined the potential for conducting comparative international studies on cancer in the aged with five registries -- two in Italy (in Trieste and Milan); one in the Slovak Republic (Bratislava); and two in Poland (in Krakow and Warsaw). In a separate exchange, the Eindhoven Tumor Registry, the Netherlands, was also visited. The focus was on the data available from these population-based tumor registries to compare with the population-based data collected by the NCI SEER Program regarding the common concerns on cancer in persons aged 65 years and older.

Our purpose was to foster scientific collaboration in the areas of mutual interest on aging and cancer relevant to geriatrics, gerontology, and oncology and to establish a regular exchange of scientific information and encourage exchange of scientists between the U.S. and each of the countries. The NIA and NCI Study Team discussed the scope and feasibility of

international collaboration on a country-by-country and registry-by-registry basis. It was not intended to develop a multi-national comparative study. Differences and similarities in the incidence and mortality rates of cancers between the U.S. and the selected nations offer insights on the high risk of acquiring cancer associated with advancing age, a phenomenon observed in the U.S. consistent with the data in Italy, Slovakia, and Poland. Our commitment to expand the knowledge base on cancer in the aged in both Institutes via appropriate tumor registries capable of cross-national research was implemented in 1992. Collaborative activities to date are:

- In December 1992, Dr. Giorgio Stanta, director of the Trieste Tumor Registry, with support from the local government, organized a scientific conference on cancer in the elderly.

- The Bratislava, Slovak Republic, Trieste, Italy, and Eindhoven, Netherlands Tumor Registries are conducting pilot studies using the NIA/NCI comorbidity form to access the medical records of older-aged patients to ascertain the logistics and feasibility of designing a prospective study similar to the NIA/NCI study.

- The Trieste Tumor Registry is characterizing the comorbidity associated with cancer in older patients revealed at autopsy and designing a study to look at the natural history of the tumor, biopsy to necropsy.

- The Trieste centenarian study is being expanded with respect to tracing the cancer burden and extending the data base to include nonagenarians (i.e., "Health and Coping Experiences in the Tenth Decade of Life").

- Studies of the prominence of multiple tumors in the elderly with the tumor registry data are underway. Multiplicity of tumors is more common in older-aged cancer patients because of the long period of development of subsequent tumors. The Trieste data, based as it is on an expansive pathology of the deceased cancer patient, has an optimum opportunity to secure this type of information.

CANCER IN AN AGING WORLD: INTERCOUNTRY VARIATIONS IN INCIDENCE, MORTALITY, AND SURVIVAL OF PERSONS 65 YEARS AND OLDER

The NIA and the NCI proposed to the International Association of Cancer Registries (IACR) colleagues that an international symposium on cancer and aging be organized. Certainly, the ideas expressed above concerning patients 65 years and older may be extended to other countries for cross-national research. The NIA Office of International Activities issued a professional services contract with IARC in August 1992, to organize and support the cancer in an aging world workshop as an adjunct to the IACR annual meeting. The current membership of IACR is about 240 cancer registries (Africa 12, Asia 33, Oceania 15, Europe, 105, North America 23, and South America 20). The IACR symposium will occur

at the September 1993 annual meeting in Bratislava, Slovak Republic. Selected papers will be published as a proceedings.

The issues to be addressed by participants in the annual meeting include:

1. What are the differences in the cancer profiles according to age for the major malignancies in a particular nation?

2. Are older-aged persons more likely to present with advanced stages of cancer at initial diagnosis?

3. Do older-aged persons receive the same type of surgical treatment procedures as younger persons?

4. What are the differences in relative survival experience of older-aged persons as compared to younger-aged persons?

5. Are data available to demonstrate associated comorbid conditions and functional status in older-aged cancer patients?

Participants in the these efforts are NIA staff, Drs. Rosemary Yancik and Richard Havlik and NCI staff, Dr. Brenda K. Edwards and Ms. Lynn A. Ries.

Resarch Highlights FY93

- The EPESE project has developed information on death, chronic conditions, disabilities, and institutionalization for representative samples of elderly people living in communities. The EPESE consists of prospective epidemiologic studies of approximately 14,000 persons 65 years of age and older in 4 different communities: East Boston, Massachusetts: two rural counties in Iowa; New Haven, Connecticut; and segments of 5 counties in the north-central Piedmont area of North Carolina. The study design includes an initial baseline household interview followed by continued surveillance of morbidity and mortality. Participants were re-contacted annually in conjunction with the collection of data on cause of death and factors related to hospitalization and nursing home admissions. Concurrently, the investigators developed substudies focused on specific problems of the elderly. The value of this research lies in the longitudinal design which allows for analyses aimed at identifying risk factors of diseases, disabilities, hospitalizations, institutionalization, and mortality. (Cornoni-Huntley, Ostfeld, Taylor, Wallace, Blazer, Berkman, Evans, Kohout, Lemke, Scherr, Korper. *Aging Clin Exp Res*, 1993;5:27-37.)

- Age comparisons for incidence, histology, disease stage at initial diagnosis, and mortality of more than 20,000 ovarian cancer patients diagnosed between 1973-1987 were the focus of this descriptive epidemiologic study. Key issues and concerns were highlighted regarding ovarian cancer in women 65 years and older as a frame of reference for the proceedings of the working conference, "Perspectives on Ovarian Cancer in Older-Aged Women," co-sponsored by NIA, NCI, and the American Cancer Society held at the NIH, November 1991. Data were from the NCI's Surveillance, Epidemiology, and End Results (SEER) Program and the National Center for Health Statistics. The SEER Program database represents approximately 9.6% of the U.S. population. Ovarian cancer affects women in the age group 65 years and older more frequently than younger women. More than 48% of all ovarian cancers occur in women in this age group. Age-adjusted rates increases as age advances, peaking at 54.0 per 100,000 in the age group 75-79 years. Time trends also indicate increases in age-specific incidence rates. This malignancy takes its toll in mortality in women 65 years and older with 64% of all deaths due to this neoplasm (in 1989). Moreover, older women are more likely to be initially diagnosed with advanced disease. Important questions about ovarian cancer in older-aged women need urgent attention from the research community. New strategies for diagnostic leads have to be developed for older women. (Yancik. *Cancer*, 1993;71:517-23.)

Epidemiology and Demography Office

The Epidemiology and Demography Office plans and conducts studies on chronic diseases and functional status and disability in the older population, with an emphasis on understanding the roles of behavioral and other risk factors and co-occurring chronic conditions on the overall health and quality of life of older persons.

Staff members work under the direction of the Office Chief, Dr. Jack M. Guralnik, with the Associate Director, other EDB Program staff members, other members of the NIA, other investigators at the NIH, Government contractors, the NCHS, and other agencies on a variety of analytical, developmental, methodological, and administrative projects.

A great deal of work this year went into the continued development of the Women's Health and Aging Study. The baseline assessments for this study began in November 1992. Work has continued on development of protocols for obtaining blood samples for a number of laboratory analyses, on the development of the follow-up and surveillance instruments, on the creation of a medications data base, and on continued training of new interviewers and maintenance of quality control for evaluations being done by nurses and interviewers.

Due to the efforts of the individual sites and the EDB Program data management staff, the Established Populations for Epidemiologic Studies of the Elderly (EPESE) has matured into a very valuable, high quality data set in the past several years. The data from these studies is now the basis for an intensive research effort by EDB Program staff working in teams and in collaboration with outside researchers. These efforts have led to a large number of papers that have been published and are under review and in preparation.

1. Women's Health and Aging Study (WHAS)

On July 1, 1991, the Johns Hopkins University (JHU) School of Medicine was contracted to perform the study over the period from July 1, 1991, through February 28, 1998. Data collection will be accomplished through a subcontract with Westat, Inc. OMB clearance was obtained in July 1992. In November 1992 field staff began screening the first of about 5,500 older women in Baltimore County and City for eligibility into the study.

A number of important hypotheses related to disability and loss of independence in older women will be addressed by this study. The project will enroll 1,000 disabled women in the study cohort who at baseline will receive an extensive baseline interview, physical examination and diagnostic tests, including a battery of tests performed on blood specimens. The baseline assessment is aimed at evaluating the major diseases and conditions of aging to ascertain their presence, severity, and impact on disability. The cohort will be followed for 3 years, with follow-up assessments every 6 months to evaluate change in disease and functional status. Members of the cohort will also be monitored for hospitalization, nursing home admission, the use of home health care, and mortality.

This study has a number of aspects that make it unique as an epidemiologic study and add substantially to previous work done on disability in older populations. Epidemiologic studies in general have tended to study factors leading to the onset of incident disease, with little study of subjects once disease occurs. This study will examine women who already have disease and disability, attempt to understand the diseases underlying that disability and then prospectively evaluate the course of disability and how the underlying diseases as well as health habits, psychological, cognitive, social and other factors affect that course. Unlike much previous epidemiologic research on disability, which has generally relied on self-reported data, this study will be able to comprehensively evaluate the association of diseases and physiologic dysfunction with disability. For example, through the use of chart reviews of previous hospitalizations, physical examinations, resting ECG's, ambulatory ECG's, pulmonary function tests, modified exercise stress tests, and oximetry readings of blood oxygen saturation both at rest and during exertion a thorough understanding is sought of the association of cardiopulmonary disease and disability in this community-based, representative sample of disabled women. Likewise, a thorough history of musculoskeletal symptoms, knee and hip x-rays, photographs of the hands, and a clinical joint examination will elucidate the association of arthritis and disability. The 6-month interval between follow-up assessments, as compared to the usual annual follow-up, should allow for a better ability to characterize change in functional status, which may fluctuate rapidly over a short period of time. A supplementary study of a subset of the participants will perform weekly assessments over a 6-month period to evaluate very short-term changes in functioning.

Additional support for the study has come from MetPath, which has provided a grant to JHU for support of blood drawing staff and supplies and will process samples at their main laboratory. In addition to routine hematology and chemistry examinations, a number of other tests are being performed, including thyroid function tests, glycohemoglobin, protein bound glucose, parathyroid hormone, various vitamin assays, and osteocalcin. Under support from MetPath these tests will be repeated at the first and second anniversaries of the baseline to provide longitudinal data for analysis. An additional grant to JHU from Merck & Co. supports blood repository personnel, equipment and supplies.

Highly sophisticated research procedures will also be performed on blood specimens from WHAS participants, at no cost to the contract, by the laboratories of several scientists who see the study as a valuable opportunity to test specific hypotheses in collaboration with WHAS investigators. Clair A. Francomano, M.D., Associate Professor, Departments of Medicine and Pediatrics, JHU School of Medicine, will perform DNA analysis to evaluate variation in candidate genes for specific common disorders of aging, including osteoarthritis and osteoporosis. Joseph B. Margolick, M.D., Ph.D., Director, Human Immune Assessment Laboratory and Associate Professor, Department of Environmental Health Sciences, JHU School of Hygiene and Public Health will evaluate sub-subsets of CD_4+ and CD_8+ lymphocytes in relation to age, frailty, and disability. Lawrence Grossman, Ph.D., University Distinguished Service Professor, Department of Biochemistry, JHU School of Hygiene and Public Health will perform an assay of DNA repair to evaluate its association with frailty and disability and change in health status over time. Robert H. Allen, M.D.,

Professor of Medicine, Division of Hematology, Department of Medicine, University of Colorado Health Sciences Center will perform assays of serum metabolites of B_{12}, including homocysteine, cystathione, 2-methyl-citrate.

The first 15 months of the study were primarily concerned with planning, development of assessment protocols, creation of an OMB package, and pre-testing of questionnaire and examination instruments. Since the baseline assessment began in November 1992, the staff at JHU, the Westat team subcontracted to collect the data, and the staff of the Epidemiology and Demography Office have continued to work intensively on other aspects of the study. All members of the Epidemiology and Demography Office, as well as Mary Lafferty and Caroline Phillips, who will participate in the data management, have made major contributions to the study. EDB Program staff function as co-investigators in this study, sit on the Steering Committee, and often take lead roles in various critical aspects of the study. Dr. Guralnik works collaboratively with Dr. Linda Fried, the Principal Investigator on the study, on the general oversight of study operations and policy.

Drs. Guralnik and Eleanor Simonsick have represented the NIA in interviewer and nurse orientation and training, providing an overview of the WHAS, its objectives, and where it fits in the Federal agenda on research and health in aging. Dr. Guralnik has trained nurses and interviewers to conduct the performance measures of functioning and provides ongoing quality control in this area. Drs. Marcel Salive, Guralnik, and Simonsick serve on the clinical disease ascertainment and surveillance committees. Dr. Salive facilitated working with the Health Care Financing Administration (HCFA) to obtain the Medicare beneficiary files for the study sampling and the Part A and B utilization data for analysis. He coordinated study efforts to obtain readings of the participant spirometry measurements from the National Institute for Occupational Safety and Health (NIOSH), Centers for Disease Control and Prevention. Dr. Simonsick has played a major role in the development of the follow-up and proxy interviews. Dr. Simonsick, working with Dr. Pearl German of JHU, is preparing the WHAS Manual of Operations, which will provide an overview of the study and the sources and references for all the data collection instruments and procedures as well as the documentation for all the analytic variables in the study. Drs. Lori Brown and Marco Pahor have directed the creation of the drug data base for the study. Dr. Brown has worked on the initiation of the laboratory studies and the documentation of the procedures used in these studies. Ms. Lafferty and Ms. Phillips serve on the data management committee.

In January, the EDB Program convened a review panel of eight distinguished scientists representing gerontology, geriatrics, social sciences, and statistics to provide oversight on the progress and future plans of the WHAS. Dr. Sidney Katz, who has played a major role in the development of geriatric research and was a pioneer in functional assessment of older persons, served as the chairman of the panel. The review covered a wide range of topics, including methods for ascertaining the presence and severity of disease, adjudicating the diseases responsible for disability, and analytic strategies. The meeting was very productive and has led to modifications in certain ongoing activities.

The design and initial data from the study will be presented at a symposium devoted to the WHAS at the American Public Health Association in October 1993.

The WHAS has begun a cooperative effort with the Baltimore Longitudinal Study on Aging (BLSA) to supplement their recruitment of African-American women. Women screened for the WHAS who do not meet the disability criteria to enter our study and who meet certain entrance criteria for the BLSA are being provided with information on the BLSA and invited to make contact with that study.

The NIA Project Officers for this study are Drs. Jack Guralnik and Eleanor Simonsick.

2. Head Injury and Alzheimer's Disease

Dr. Salive has developed a Request for Proposals for a study to determine whether head trauma increases the risk of Alzheimer's disease, which has been announced in the Commerce Business Daily. Proposals were received in July 1993 and an award may be made in early FY 1994. An earlier pilot study, conducted by the Institute of Medicine Medical Follow-up Agency (MFUA), determined the feasibility of performing this study.

3. Established Populations for Epidemiologic Studies of the Elderly (EPESE)

The three original community populations comprising the EPESE are located in East Boston, Massachusetts; Iowa and Washington Counties, Iowa; and New Haven, Connecticut. Baseline data collection began in December 1981, and annual interviews were conducted either in-person (third and sixth years of follow-up) or by telephone (first, second, fourth and fifth years of follow-up) for 6 years following the baseline. A 5-year extension contract was awarded to each of the three original EPESE cohorts in February 1989. The extensions place major emphasis on data clean-up and to continued monitoring of mortality through the National Death Index and to monitoring hospital utilization through linkage to Medicare records from the HCFA. In the past year, links to Medicare records have been successfully completed and the quality and utility of the information obtained appears quite good. Analyses have begun that use these linked records to document hospitalization for specific events and costs of hospitalization.

While contract closeouts for the original three EPESE sites will occur this calendar year, intensive research efforts will continue.

Dr. Guralnik continues as Project Officer for the Iowa 65+ Rural Health Study at the University of Iowa. The study was awarded a research grant from the Behavioral and Social Research (BSR) Program at NIA to perform a 10-year follow-up assessment. This has been completed and data are now being readied for research. Staff at Iowa will continue to collaborate with EDB Program staff on analyses of these data.

Ms. Mary Lafferty, Data Manager in the Biometry Office, is the Project Officer for the East Boston Senior Health Project (contractor, Brigham and Women's Hospital). Mr. Daniel Foley, Statistician in the Biometry Office, is the Project Officer for the Yale Health and Aging Project (contractor, Yale University). Updates of these two contracts can be found in the Biometry Office section of this Annual Report.

The Piedmont Health Survey of the Elderly (PHSE) was added as the fourth site of the EPESE project in 1985. In this fourth site, Duke University has established a sample of 4,164 people 65 years of age and older, 54 percent of whom are black. This cohort is the only southern EPESE population, constitutes a representative sample of the elderly in five North Carolina counties, and includes both urban and rural participants. The baseline survey for this site began in January of 1986 and was completed in June 1987. There have been five annual follow-up evaluations completed since then. A new 7-year contract was awarded to Duke University Medical center January 1, 1991, to conduct a third in-person survey wave and continue surveillance for major endpoints using the National Death Index and HCFA hospitalization data tapes after direct contact with subjects is completed. The third in-person follow-up will be completed shortly. Duke is gathering information comparable to that obtained by the other sites, including physical performance measures and blood samples, and also will include items which are important for the study of the health of older black persons and racial and urban/rural differences. Dr. Dwight Brock is the Project Officer, and further information is in the report of the Biometry Office.

Epidemiology and Demography Office staff were involved in the following EPESE data analysis activities:

Drs. Salive and Guralnik have helped to resolve the issue of whether left-handed individuals have a higher mortality than right-handers (see Research Highlights). An analysis of East Boston EPESE data demonstrated no difference in mortality by handedness. These results, which were published in the American Journal of Public Health, were the subject of an NIA press release that resulted in articles in the Washington Post, LA Times, New York Times and a cover story in USA Today. The research also received extensive local, national and international radio and magazine coverage.

Drs. Salive and Karen Collins (a Johns Hopkins Preventive Medicine Resident) completed a collaborative analysis, with Dr. Linda George of Duke University and Dan Foley of the Biometry office, of the predictors of nursing home admission in the North Carolina EPESE population. Age-adjusted 3-year incidence rates of nursing home admission were 8.5 percent for whites and 6.4 percent for African-Americans. The racial differences in nursing home utilization were not explained by disability, cognitive impairment or measures of financial access and social support. These results were presented at the Gerontological Society of America 1992 annual meeting and accepted for publication in the American Journal of Public Health.

Drs. Salive and Guralnik evaluated the association of physical function with visual impairment in cross-sectional and longitudinal analyses. After controlling for potential confounders, persons with severe visual impairment had a higher odds of incident mobility and activity of daily living (ADL) limitations than those with acuity of 20/40 or better. Those with poor vision were less likely to improve their physical function than those with better acuity; this was statistically significant only for improvement in mobility. Distant vision appears to play an important role in physical function, particularly mobility. An intervention to improve vision in at-risk elders might preserve physical function and prevent disability. A manuscript has been submitted for publication.

Dr. Salive recently completed a longitudinal analysis with Dr. Dan Blazer of Duke University that explores the relationship of smoking cessation and depression in the North Carolina EPESE. Current smokers had the highest prevalence of clinically significant depressive symptoms, followed by never smokers and former smokers. Depressive symptoms were significantly associated with nearly fourfold increased odds of smoking cessation among women, but not among men, after adjusting for potential confounding. This challenges prior reports that depressed smokers are less likely to quit smoking than nondepressed smokers. These results have been accepted for presentation at the 1993 meeting of the American Public Health Association and submitted for publication.

Dr. Salive is collaborating with Dr. Camille Jones of the NIDDK on a descriptive analysis of serum creatinine in the EPESE participants who had blood drawn for testing. Variables of interest include age, gender, history of hypertension and diabetes. This follows up on an analysis by Salive and Havlik, published as a letter to the editor in JAMA, which looked at the predictive power of current blood pressure and blood pressure 6 years earlier for serum creatinine. A manuscript is being prepared.

Drs. Salive and David Stein performed an analysis of EPESE data on alcohol consumption and its relation to melanoma. A brief manuscript is being prepared for submission to the dermatological literature.

Drs. Simonsick, Guralnik, and Harris are conducting an analysis and preparing a manuscript on "The natural history of physical vitality in 71 to 85 year olds." Healthy aging is a highly desired individual and societal objective. Most studies of healthy aging focus on the maintenance of physical function and typically define healthy aging as the absence of physical disability and limitation. These criteria distinguish the top 30 to 50 percent - the usual, but not necessarily the successfully aged. Using data from 2,505 persons age 71 to 85 years at the sixth year followup from the East Boston, New Haven and Iowa sites, this study compares the "usual" and the "vital" aged. The usual aged consist of persons with no self-reported ADL disability or mobility limitation. The vital meet criteria for usual aged and score 10 or more on a 12-point summary scale of three performance-based measures of physical function. This study aims to identify behaviors; cognitive, psychological and social factors; and health conditions associated with physical vitality both cross-sectionally and 6 years previous. Cross-sectional comparisons reveal few differences between the vital and

usual aged with regard to disease history, although the vital are more likely to rate their health excellent and less likely to rate their health poor or worse. The vital show consistently fewer errors on a test of cognitive function. Vital females exhibit consistently lower rates of depression, are less likely to be overweight and more likely to report group membership. This paper has been accepted for presentation at the Gerontological Society of American meetings to be held in November 1993.

Dr. Simonsick is preparing a chapter on the Demography of Productive Aging. Data from the New Haven and Iowa sites were used to provide estimates of participation in leisure and recreational activities among older persons by gender, age group, health status and educational attainment.

Together with Dr. Jane Pearson from NIMH and Ms. Phillips, Dr. Simonsick is performing analyses and preparing a manuscript examining death by suicide in the four EPESE sites. While only 18 cases have been identified, the EPESE data provide a rare opportunity to examine prospectively factors associated with suicide in older adults. In addition to demographic features and depressive symptoms, health and functional decline will be examined in detail. Consistent with national rates, all suicides were male and all but one were white race. Preliminary analyses found rates of widowhood, physical impairment, smoking and high depressive symptoms much higher among the suicides than the base community populations. This paper has been accepted for presentation at the Gerontological Society Meetings in November 1993.

Drs. Simonsick and Guralnik, in collaboration with Drs. Charles Hennekens, Robert Wallace, and Adrian Ostfeld, have submitted for publication "Intermittent claudication and subsequent cardiovascular disease in the elderly." This study reports the prevalence of intermittent claudication (IC) in ambulatory community resident adults age 65 years or older, compares cardiovascular risk factors and comorbidity of persons with and without IC, and examines the independent association of IC in predicting all cause and cardiovascular mortality, myocardial infarction, stroke and disability. Data are from a pooled sample of 8,996 older adults from the East Boston, New Haven and Iowa EPESE. 2.4 percent and 1.5 percent of males and females, respectively reported IC. Persons with IC had significantly higher rates of diabetes and cardiovascular comorbidity than persons without IC and were more likely to smoke. Claudication predicted higher rates of mortality, myocardial infarction, stroke and disability independent of associated cardiovascular conditions and risk factors. Among persons with a history of angina, myocardial infarction and/or stroke, those who also reported IC had a 2-fold greater risk of cardiovascular mortality. The study demonstrated that IC is an important predictor of mortality and cardiovascular morbidity in ambulatory older adults independent of associated coronary ischemia and cardiovascular disease risk factors. Results suggest that inclusion of a measure of IC improves the prediction of cardiovascular morbidity and mortality in older adults. An earlier version of this paper was presented at the 1992 annual meeting of the American Public Health Association.

Dr. Simonsick with Drs. Wallace, Blazer, Glynn and Berkman has updated the analyses, completed and submitted the manuscript examining depressive symptomatology and hypertension associated morbidity and mortality in older adults. This paper used data from the East Boston, Iowa, and New Haven sites. The study population consisted of persons who had been told they have high blood pressure and at baseline had measured systolic blood pressure above 160mm Hg or diastolic blood pressure above 95mm Hg or were taking medication for their blood pressure. Depressive symptomatology was measured with the original or a modified version of the CES-D. Scores from the modified forms were transformed to determine cutpoints analogous to a score of 16 on the original scale. Analyses were stratified by sex and site and compared persons with high and low depressive symptomatology. Hypertensive females with high depressive symptomatology showed significantly greater all cause and cardiovascular related mortality after 6 years. Depressed males and females showed 2- to 3-fold higher rates of stroke after 3 years. As depression often responds well to treatment, recognizing and understanding its role in the development of more severe disease is highly desirable.

Dr. Simonsick is performing analyses that examine the demographic, health and functional characteristics of persons age 65 to 69 years who are still working in comparison to persons in the same age group who are no longer working, including and excluding persons who stopped working due to disability. The analysis follows this population of older workers for 5 years to prospectively evaluate factors associated with retirement and continued working, primarily from a health status and health event prospective. A primary assumption is that any event that occurs in a follow-up period precedes a change in work status. The major hypothesis is that persons who are still working at age 65 years and beyond will continue to work until they no longer have the physical or mental capacity to do so. This will be related to occupational type as different occupations have different physical and cognitive demands. Social factors such as the loss of a spouse may also be related to continued working. The analyses are done separately for men and women within each EPESE site. While many studies examine predictors of retirement, few examine factors associated with continued working among persons of retirement age.

Dr. Simonsick, with Dan Foley and Dr. Andrew Monjan of the Neuroscience and Neuropsychology of Aging (NNA) Program, is collaborating on an analysis of "Sleep complaints and insomnia among elderly persons: Data from the Established Populations for Epidemiologic Studies of the Elderly."

Dr. Simonsick is collaborating with Kathy Lozonscy and Drs Harris, Cornoni-Huntley, Wallace, Cook, Ostfeld, and Blazer on "Does weight loss from middle to old age explain the inverse weight mortality relation in old age?"

Drs. Lori Brown, Marcel Salive, and Jack Guralnik have completed an analysis of the effect of depression in the EPESE population on the white blood cell count. Their study demonstrated that there was an increase in the number of white blood cells in those whose scores on the Centers for Epidemiologic Studies Depression (CES-D) Scale was in the top

decile. Because other factors such as chronic illness and smoking might contribute to the changes in leukocyte count, linear regression models adjusting for these and other factors were also performed and indicated that even after adjusting for possible confounders, there was still a difference in the leukocyte count in those elderly participants who had high scores on the CES-D when compared to those who did not. The results of this study have been submitted for publication and have been presented at the NIH Research Festival in September 1993.

Drs. Brown, Harris, Salive, Guralnik, and Simonsick have completed an analysis which examines the purported association between low plasma cholesterol and depression in the elderly. A recent study suggested that although the benefits of low cholesterol in preventing heart disease were clear, these benefits were offset by an increased risk in those with lower cholesterol because of increases in death due to external causes: murder, suicide, and accidents. Another study suggested that this could be due to an association between low cholesterol levels and depression. However, an alternative explanation for these findings could be confounding by factors associated with low cholesterol such as weight loss due to illness which could promote depression and reduction in plasma cholesterol levels. Using data from the EPESE studies, this hypothesis was tested. After adjusting for factors related to illness such as number of medications taken, weight loss, and difficulties in performing activities in daily living there is no significant association between low serum cholesterol levels and high depressive symptoms in the elderly. A manuscript describing the results of this study has been prepared and will soon be submitted for publication.

Drs. Brown, Salive, Guralnik and Pahor have started an analysis of the use of antidepressants and their correlates at the four EPESE sites. Preliminary analysis indicates that the use of antidepressants was not associated with age, marital status, level of education or income. However there was an association of antidepressant use with sex and with race. Women and non-blacks were more likely to be using antidepressant medication. Further analysis is planned to determine if these associations hold after more complex analysis weighting the data at the different sites according to their sampling tactics. The preliminary results of this study have been submitted to the Gerontological Society of America and will be presented in the Clinical Medicine Section.

Drs. Brown, Salive, Guralnik, and Ms. Caroline Phillips are planning an analysis of the long term outcomes of antidepressant use in the EPESE populations. This study will examine the outcomes of antidepressant use in the elderly with respect to health outcomes over the next 3 years. This will be achieved using information from the Medicare hospitalization files in conjunction with EPESE follow-up data to ascertain whether there are differences in health outcomes for those who are taking antidepressants compared to those who are not.

Drs. Guralnik, Simonsick and Luigi Ferrucci have continued work on the performance measures of functioning collected at the sixth annual follow-up. Dr. Guralnik presented results from these analyses at the Gerontological Society of America meeting in November 1992 in Washington, at a meeting of Spanish investigators in Madrid in April 1993, and at a

meeting on the use of performance measures in Boston in May 1993. Numerous investigators from the U.S. and abroad have expressed interest in using these measures in their research and have been provided personal consultation and supplied with the study protocols and the videotapes used to train the EPESE interviewers that were produced jointly by NIA and the MacArthur Foundation. A paper on the performance measures, titled "A short physical performance battery assessing lower extremity function: Association with self-reported disability and prediction of mortality and nursing home admission" has been accepted for publication in the Journal of Gerontology, Medical Sciences. This paper, in addition to its analyses, includes an appendix containing the distributions of the performance test results by sex and age group that will provide normative values for these tests for all investigators who use the EPESE instrument.

Dr. Guralnik, in collaboration with investigators at Duke University, has continued work on the methodology of computing active life expectancy according to various covariates such as race and educational status. The first results of this work were published in the New England Journal of Medicine in July. Dr. Guralnik and Dr. Ken Land of Duke have submitted a paper to Demography that provides details of the analytic procedures for these computations titled "On the estimation of increment-decrement life tables with multiple covariates from panel data: The case of active life expectancy."

Dr. Guralnik has developed analyses to investigate the relative impact of chronic conditions on both mortality and disability. This research adds to the work on the association of chronic conditions with incident disability in the EPESE cohorts that was recently published in the American Journal of Epidemiology by investigating, using the same methodology, the impact of these same conditions on mortality. This research was presented in July 1993 at the World Congress of Gerontology in Budapest.

Drs. Pahor and Guralnik have completed work using data from the Iowa EPESE population on the use of laxatives in the older population. The prevalence of laxative use was 8.8 percent in the community dwelling population and 74.6 percent in nursing homes, with increasing age associated with greater use. Types of laxatives used in the community and in institutions were documented. Laxative use was found to be independently associated with an increased rate of hypoalbuminemia after adjusting for age, sex, anemia, number of comorbid conditions, disability in activities of daily living, body mass index, and use of other drugs that were associated with hypoalbuminemia. This report has been submitted for publication.

Drs. Ferrucci and Guralnik have begun an investigation of the impact of stroke on functional status in the EPESE cohorts. This work complements previous research done by Drs. Ferrucci and Guralnik on functional outcome after stroke rehabilitation in an Italian cohort. That research was published in Stroke in February 1993.

Drs. Pahor, Guralnik, and Brown have completed work on a paper outlining the classification systems for drug data collection and analysis in epidemiologic studies.

Although many epidemiologic studies collect drug data, there have been a limited number of satisfactory systems developed to code and analyze the data. Examples of a European and an American system (developed for the EPESE study) that meet the criteria proposed for effective classification systems are presented in this paper, with examples of how these systems code certain drugs. This paper will be submitted to the American Journal of Epidemiology.

Drs. Pahor, Guralnik, and Salive have pursued analyses using the Medicare records of EPESE participants to identify those who had hospital admissions for gastrointestinal hemorrhage. Both rates and risk factors for this condition are being explored.

Drs. Antonio Sgadari, Guralnik, and Simonsick have completed a study that develops criteria for judging the validity of self-reported measures of functioning across countries. These criteria, which focus mainly on predictive validity for mortality, are applied to measures of functioning in an Italian cohort in Molise, in south-central Italy, and the four EPESE cohorts. After items that are validated across sites are combined into a scale of functioning, disability and higher level functioning are compared for the different communities. This paper will be submitted for publication shortly.

Drs. Sgadari, Guralnik, and Salive have done developmental work on the creation of a hierarchical scale of functioning that is valid across communities and countries using data from the Molise study and the EPESE.

4. Analytic and Developmental Accomplishments by Epidemiology and Demography Office staff.

Dr. Salive served as the Public Health Service Delegate to the American Medical Association Young Physicians Section, representing the Service to the annual and interim meetings 1992-1993 and serving on a Reference Committee at the 1993 annual assembly.

Dr. Salive was selected to serve on the Governing Board of the American Journal of Preventive Medicine, 1992-95.

Dr. Salive is serving on the Planning Committee for Prevention '94, a national meeting cosponsored by the NIH and sponsored by the American College of Preventive Medicine and the Association of Teachers of Preventive Medicine.

Dr. Salive served as a manuscript reviewer for the following professional journals: Military Medicine, American Journal of Public Health, and Schizophrenia Bulletin. He also reviewed papers written for the User Liaison Program of the Agency for Health Care Policy and Research.

Dr. Salive served as a scientific reviewer for Racial & Ethnic Populations contract proposals submitted to the National Center for Health Statistics.

Drs. Salive and Guralnik, in collaboration with Dr. Brock of the Biometry Office, have undertaken a study to examine delivery of preventive services for breast and cervical cancer and the bundling of several preventive services using data from the National Ambulatory Medical Care Survey on visits by women age ≥ 45 yrs to office-based physicians during 1989 and 1990. The periodic preventive visit has received only limited acceptance by physicians who provide preventive care for adult women. Payment for preventive visits changes with age and may affect the appropriate provision of services. The results were presented at Prevention '93 (the national meeting of the American College of Preventive Medicine) and the report was covered in the American Medical News. A manuscript has been submitted for publication.

Dr. Salive provided consultation and collaboration with Dr. Carol Bazell of Johns Hopkins University on a commentary article describing physicians who were dually trained in pediatrics and preventive medicine during the 1980s. Dually trained pediatrician/preventive medicine specialists are well equipped to meet the challenges called for by health policy makers who recommend training primary care physicians in population-based medicine, with an emphasis on disease prevention and health promotion. The paper was submitted for publication.

Drs. Salive and Stein have made a contribution to understanding the training of preventive medicine residents, using data from a national survey. The quality of training in the core areas of preventive medicine (epidemiology, health administration and policy, clinical preventive medicine, occupational medicine and environmental health) varies primarily according to the residency sponsorship and the setting in which training takes place. Critical weaknesses were noted for training in health administration in general and for occupational and environmental health among residents who spend <2 months working in a health department. The manuscript is being revised for submission.

Dr. Salive provided consultation and collaboration with Dr. Andrew Dannenberg and others of Johns Hopkins University on an analysis of correlates of preventive medicine board certification, in a study of 10 years of residency graduates. Influential factors include residency sponsor, perception of a benefit for certification, absence of certification in another clinical specialty, and race/ethnicity. The manuscript is being revised for submission.

Drs. Simonsick and Brock contributed to the development of the informant survey component of the 1994 Mortality Followback Survey. Dr. Simonsick has been involved in selecting the questions and instruments for the assessment of physical and cognitive functioning and mobility limitations prior to death. Additionally, Dr. Simonsick developed a new set of questions designed to ascertain physical, social, and intellectual activities in the year prior to death.

Using a subset of the Honolulu Heart Project cohort, Dr. Simonsick is collaborating with Drs. Harris, Havlik and White to develop a study examining weight, weight history, and body composition and their association with indicators of health status, possibly glucose tolerance. A second set of analyses will examine change in cognitive function in relation to physical activity patterns and occupational status and activities.

Dr. Simonsick is collaborating with Julie Weeks and Drs. Harris and Kovar on a paper designed to address risks associated with functional limitation. Data are from all four waves of the Longitudinal Study on Aging (LSOA). This paper was accepted for presentation at the Gerontological Society Meetings, November 1993.

Dr. Simonsick serves as a consultant to the Health and Retirement Study Monitoring Committee. The Health and Retirement Study (HRS) is being conducted by the University of Michigan as a cooperative agreement with the NIA's Behavioral and Social Research Program (BSR). The objective of the HSR is to describe the economic, health and other factors that influence retirement decisions as well as to track changes in health status and economic well-being as the panel ages. It is designed as a longitudinal survey of a large national sample of individuals approaching retirement age. Preliminary data became available in July 1993.

Dr. Simonsick is a member of the Community Prevention Study (CPS) working group of the Women's Health Initiative (WHI). The WHI is a broad ranging research program designed to evaluate the effects of preventive interventions on cancer, cardiovascular disease and osteoporosis in women. The CPS component of the WHI aims to identify effective ways of achieving healthful behaviors related to dietary pattern, nutritional supplementation, hormone replacement therapy, smoking cessation and prevention, physical activity and cancer detection. In early 1993 the CPS underwent a major overhaul and is back in the development stage. Dr. Simonsick reviewed and revised the component related to physical activity.

Dr. Simonsick developed a study of "Indicators and determinants of physical and cognitive vitality in old age". This initiative is designed as an add-on study to a community sample for which basic data on physical functioning has been collected and aims to identify physiologic and behavioral factors that distinguish the exceptional from the usual aged, both physically and cognitively. The study also aims to assess intellectual capacity, determine the association between cognitive and physical vitality, and identify factors associated with the maintenance of cognitive function over time.

Dr. Simonsick contributed to the concept development of "Dynamics of Health, Aging and Body Composition (Health ABC)" with Dr. Harris.

Drs. Brown and Guralnik provided consultation and documentation on the use of the EPESE drug data base to Dr. Dwayne Reed of the Buck Center for Research in Aging.

Drs. Pahor and Brown consulted with Dr. Mary Forbes at the FDA on the availability of drug databases for use in research and analysis.

Drs. Ferrucci and Guralnik completed a paper titled "The role of cognitive impairment in the pathway from disease to disability," which has been accepted by Aging, Clinical and Experimental Research. This research demonstrates that common chronic medical conditions can have a direct effect on cognitive functioning and that this decline in cognitive functioning plays a role in how these disease cause disability.

Drs. Guralnik and Havlik completed an overview of important epidemiologic and demographic issues in the older population. This work will be published as a chapter in the second edition of The Merck Manual of Geriatrics.

Drs. Havlik and Guralnik, in collaboration with Dr. Adrian Ostfeld of Yale University, completed work on a chapter titled "Epidemiology of Hypertension in the Elderly" for a major reference text in the field of hypertension, Hypertension: Pathophysiology, Diagnosis, and Management, edited by Laragh and Brenner.

Dr. Guralnik, working together with Dr. Carol Winograd, Chief, Clinical Programs in Geriatric Medicine, Stanford University School of Medicine and Dr. Stephanie Studenski, Director, Center on Aging, University of Kansas Medical Center, organized and funded a meeting on performance measure of physical functioning in Boston in May 1993. Major contributors to geriatric research who have had experience with these instruments were invited to attend this meeting and were presented with the challenge of clarifying the appropriate use and selection of performance measures. There is a growing interest in the use of these measures to replace or supplement the information traditionally obtained from self-report measures of disability. The field has grown rapidly in just a few years and the meeting served as a valuable forum to review the entire field at this juncture. In particular, performance measures are beginning to be used as outcome measures in intervention trials aimed at improving function in the older population, but more work needs to be done to fully appreciate their strengths and weaknesses. A paper reviewing the recommendations of the working groups that met during the meeting is now in preparation.

Drs. Pahor and Guralnik completed work on a study of adverse drug reactions to digoxin, using data from a multi-center pharmacosurveillance study organized by Dr. Pahor in Italy. In this study, increasing age, elevated serum creatinine, daily digoxin dose $\geq$ 0.25 mg., and treatment with specific drugs increased the risk of digoxin toxicity. After controlling for a number of important covariates it was found that compared to those less than age 65, being in the age group 65 to 74 was not an independent risk factor for developing digoxin toxicity but being age 80 and older was an independent risk factor. A manuscript has been accepted by the Journal of Clinical Epidemiology.

Drs. Guralnik and Havlik have begun work examining international demographic trends in population growth, life expectancy, and mortality, with a special focus on trends in heart disease mortality throughout the world. This work will be presented at the World Health Organization meeting on epidemiology and prevention of cardiovascular disease in the elderly in October 1993 in Geneva.

Dr. Guralnik and Dr. Stefania Maggi of the World Health Organization Special Program for Research in Aging completed research comparing self-reported and performance measures of functioning in the Veneto region of Italy with the EPESE studies. Results of this research were presented by Dr. Maggi at the Gerontological Society of America meeting in November 1992 and by Dr. Guralnik at the World Congress of Gerontology in Budapest July 1993. Comparing measures that were administered in the same way in both countries it was found that the Italian cohort self-reported less disability but did consistently worse on the objective performance tests. The reason for these differences was not clear. In comparing the outcomes of the performance tests in the two countries, the differences were not explained by differences in age distribution, living situation, educational status, or self-reported health status.

Drs. Ferrucci and Guralnik have completed analyses on foot pain in an older cohort of Italians who were examined by physicians and evaluated for the causes of their foot pain and the impact of the pain on functional status. It was found that foot pain was an independent predictor of disability, even after controlling for other chronic conditions and demographic characteristics. This paper will be submitted for publication shortly.

Dr. Guralnik serves on the Editorial Boards of the Journal of Aging and Health and the journal Revista de Gerontologia, published in Barcelona, Spain. He reviews papers for a number of journals, including the New England Journal of Medicine, the Journal of Gerontology, the American Journal of Public Health, and the Journal of the American Geriatrics Society.

Dr. Guralnik lectured on the impact of chronic disease in the older population in the course Introduction to Gerontology at the Johns Hopkins University School of Hygiene and Public Health.

Dr. Guralnik consulted with the Patient Outcomes Research Team (PORT) on Hip Fracture Repair and Total Hip Replacement at the University of Maryland on the measurement of change in functional status after hip fracture.

Dr. Guralnik is consultant to a project on the financial and medical impact of rationing high technology health care in the older population, Principal Investigator Dr. Edward Schneider, Dean, Andrus School of Gerontology, University of Southern California. Recent work has evaluated trends over the last decade in hospital discharges for the most common hospital

procedures performed on older persons and uses data from the National Hospital Discharge Survey. This project is funded by the Retirement Research Foundation.

Dr. Guralnik has continued his collaboration with INRCA, the Italian National Research Institute on Aging Care, on the follow-up of the European Eleven-Country Study of the Elderly. He attended a meeting of investigators from seven of the original countries who have done follow-up evaluations on their cohorts in Florence in October 1992 to consult on the analyses of these data. In his consultant capacity he also proposed a new name for the study, which was unanimously accepted by all participating countries. The study is now know as the European Longitudinal Study on Aging (ELSA). Dr. Guralnik was co-author of a paper presented in a symposium on ELSA at the World Congress of Gerontology in Budapest in July 1993.

Dr. Guralnik has offered continuing consultation to researchers from several universities in Spain who are beginning epidemiologic studies addressing various health problems in the older population. In December 1992 he travelled to Madrid to consult with Dr. Victoria Zunzunegui and her staff at the Centro Universitario de Salud Publica on a study similar to the EPESE for which they were preparing. This study, titled "Maintaining the Quality of Life in the Elderly by Maintaining them in their Community" will examine a representative population in a small city outside of Madrid. Through the efforts of Dr. Guralnik, an American corporation, the Welch-Allyn Company, has consented to loan to the study audioscopes, instruments used to screen for hearing loss.

Dr. Guralnik is consulting with Dr. Ashlesha Tamboli, of the NIA Geriatrics Program, on a workshop she is planning on functional independence in the elderly. The workshop will focus on the clinical trial methodology in this area.

Dr. Guralnik was a keynote speaker and participated in a conference on the compression of morbidity held at NIH in February 1993. The conference was sponsored by Dr. Mary Haan, Director of the Center for Aging and Health, University of California School of Medicine, Davis, and was funded by Dr. Richard Suzman of the Behavioral and Social Research Program at NIA. The title of Dr. Guralnik's address was "Scenarios for the Compression of Morbidity: What Can We Learn From Studying Disabled Life Expectancy in Current Subpopulations."

Dr. Guralnik returned to Madrid in April 1993 to participate in a meeting of the Spanish Working Group on Aging Research. The group is comprised of investigators who are funded by the Fondo de Investigacion Sanitaria (FIS, Fund for Health Research, the research arm of the Ministry of Health) to do population-based epidemiologic studies of aging. In addition to Dr. Zunzunegui's study, there were four other groups from across the country represented. Research projects for these groups include a study of neurologic diseases in urban and rural populations, a study of heart disease and stroke, and two studies assessing chronic diseases, health and functional status in older persons in Madrid and Barcelona. The purpose of the meeting was to select certain core instruments that will be used across their studies. Dr.

Guralnik spoke on the American experience in the assessment of functional status and, following the meeting, provided the group with formal recommendations for the assessment of physical functioning through the use of both self-report and performance measures.

Dr. Guralnik lectured to the U.S. Public Health Service Epidemiology Training Program fellows on the epidemiology of aging.

Dr. Guralnik serves as EDB Program representative to the MacArthur Project on Successful Aging. He led a research effort to evaluate whether performance measures of functioning can serve to accurately represent the hierarchy of functioning in individuals at the high end of the functional spectrum, and a paper on this work is now under review. Dr. Guralnik also collaborated with Dr. Teresa Seeman of Yale University and others on a paper analyzing change in functional status in this cohort, which has been accepted for publication the Journal of Gerontology, Medical Sciences.

Dr. Chiara Corti, Visiting Fellow since June 16, 1993, is collaborating with Dr. Trudy Bush of the Department of Epidemiology, School of Hygiene and Public Health, The Johns Hopkins University, in a study to investigate the role of albumin levels in predicting cardiovascular mortality in the Florida Geriatric Research Program population. Low serum albumin levels seem to be inversely associated with all cause and cardiovascular mortality in the elderly. This association needs to be further explored and analyzed among different populations.

Dr. Corti presented a review on cardiovascular risk factors in the elderly at the XV World Congress of Gerontology in Budapest. The presentation was held on July 5, 1993, during a round table on "Blood Lipids and Cardiovascular Aging."

5. Talks and Presentations

Guralnik JM. Performance measures of function in the evaluation of older populations. Presented at the Drug Information Association Workshop "Epidemiology and the Evaluation of Medical Interventions," Baltimore, October 1992.

Guralnik JM, Land K, Blazer D, Fillenbaum G, Branch L. Active life expectancy: an approach to estimation for sex, race, and educational status subgroups. Presented at the 120th Annual Meeting of the American Public Health Association, Washington, D.C., November 1992.

Guralnik JM, Simonsick E, Ferrucci L, Berkman L, Blazer D, Glynn R, Scherr P, Wallace R. Do performance measures add to our understanding of older persons' functional status? Presented at the 45th Annual Scientific Meeting of the Gerontologic Society of America, Washington, D.C., November 1992.

Guralnik JM. Methodological issues in evaluating predictors of functional status in older populations. Presented at the Centro Universitario de Salud Publica, Madrid, Spain, December 1992.

Guralnik JM. Evaluating functional status in epidemiologic studies in older populations. Presented at the Spanish Ministry of Health meeting of the Spanish Working Group on Aging Research, Madrid, Spain, April 1993.

Guralnik JM. Measuring the spectrum of physical functioning and disability in older populations. Presented at the XVth International Congress of Gerontology, Budapest, Hungary, July 1993.

Guralnik JM. The epidemiology of longevity: Differential effects of important chronic conditions of aging on disability and mortality. Presented at the XVth International Congress of Gerontology, Budapest, Hungary, July 1993.

Salive ME, Guralnik JM, Christen W, Glynn RJ, Ostfeld A. Visual Functioning in Older Adults from Three Communities. American Public Health Association 120th annual meeting, Washington, D.C., November 9, 1992.

Salive ME. Functional Blindness and Visual Impairment in Older Adults from 3 Communities. Gerontological Society of America scientific meeting, Washington, D.C., November 19, 1992.

Collins KS, Salive ME, George LK, Foley DJ. Do Predictors of Nursing Home Admission Explain Racial Differences? Gerontological Society of America scientific meeting, Washington, D.C., November 19, 1992.

Salive ME. Delivery of Preventive Services in Office-based Practice. Prevention '93 (American College of Preventive Medicine national meeting), St. Louis, April 18, 1993.

Salive ME. Established Populations for Epidemiologic Studies of the Elderly. Drug Information Association, 29th annual meeting, Chicago, July 13, 1993.

Salive ME, Guralnik JM. Compression of Disability? Results from the Established Populations for the Epidemiologic Study of the Elderly. National Center for Health Statistics Public Health Conference on Records and Statistics, Bethesda, MD, July 19, 1993.

Salive ME. That all would live long, but none would be old. NIH Research Festival, Bethesda, September 22, 1993.

Simonsick EM, Guralnik JM, Hennekens CH, Wallace RB, Ostfeld AM. Is intermittent claudication an independent predictor of subsequent morbidity and mortality in the elderly.

Presented at the 120th Annual Meeting of the American Public Health Association, Washington, D.C., November 1992.

Simonsick EM. The Demography of Productive and Successful Aging. Presented at the Vermont Conference on the Primary Prevention of Psychopathology (VCPPP) - Promoting Successful and Productive Aging, Burlington, VT, June 9-12, 1993.

6. New and Visiting Staff

Chiara Corti, M.D., M.H.S. joined the Epidemiology and Demography Office June 16, 1993, as a Visiting Fellow. Dr. Corti is a geriatrician from the University of Padua, Italy, who has done clinical and laboratory research on serum lipids. She spent the past year earning an M.H.S. degree in epidemiology at The Johns Hopkins School of Hygiene and Public Health. Dr. Corti will remain with the office for 1 to 2 years.

David Stein, M.D., M.P.H. spent 3 months with the Office from March through May. Dr. Stein, a board certified dermatologist, is a resident in preventive medicine at Johns Hopkins University.

Marco Pahor, M.D., from the Division of Gerontology of the Universita Cattolica del Sacro Cuore in Rome, was a Guest Researcher in the Exchange Scientist Program from July through November 1992. Dr. Pahor is a geriatrician with extensive experience in clinical and laboratory research who has begun doing epidemiologic investigations in the past few years. His main area of interest and expertise is in pharmacoepidemiology. He will return as a guest researcher from July through October.

Antonio Sgadari, M.D., spent 3 months with the Office from May through July as a Guest Researcher. He is a geriatrician with the Division of Gerontology of the Universita Cattolica del Sacro Cuore in Rome and has had previous experience in clinical research and epidemiology.

Luigi Ferrucci, M.D., Ph.D., from the Italian National Institute on Aging and the Ospedale I Fraticini in Florence has been a Guest Researcher and Visiting Associate during two previous extended visits. He will return for a short visit in November 1993 and for an additional extended visit in 1994. He has continued to perform collaborative research with EDB Program staff during his absence. Dr. Ferrucci is a geriatrician with experience in clinical and epidemiologic research.

7. Honors and Awards

Dr. Salive was awarded the U.S. Public Health Service Achievement Medal for "exceptional production of scientifically significant publications with potential applications to health promotion and disease prevention strategies for older persons." He received a medal with ribbon at the NIA Employee Recognition Day, September 23, 1993.

Research Highlights FY93

- This study describes the long-term evolution of self-reported functional ability after discharge from rehabilitation, and its relationship with age, level of neuromuscular impairment at discharge and changes in neuromuscular impairment over the follow-up. Fifty patients (31 men and 17 women; mean age 66.0$\pm$9.9 years, range 47-86) with a first unilateral stroke and no severe cognitive impairment were consecutively enrolled. Self-reported disability in activities of daily living and neuromuscular impairment measured by the Fugl-Meyer Scale were evaluated after discharge from a rehabilitation program and 3 and 6 months later. Both functional disability and neuromuscular impairment were significantly reduced after 3 and 6 months. Attenuation of disability occurred mainly among those with more severe baseline neuromuscular impairment. In this group, patients aged $\geq$65 years were more disabled at baseline than younger individuals, but they had the same slope of improvement. In those aged $<$65 years, changes in disability over time could be entirely attributed to changes in neuromuscular function, whereas older patients' functional recovery was greater than that expected from their improvement in neuromuscular impairment alone. These results suggest that in stroke patients with severe neuromuscular damage further functional improvement occurs even after completion of a rehabilitation program. There is evidence that older patients may be more likely to employ compensatory strategies to overcome some of the neuromuscular impairment that remains following stroke. (Ferrucci, Bandinelli, Guralnik, Lamponi, Bertini, Falchini, Baroni. *Stroke* 1993;24:200-205).

- This study reports data on performance in two tests of balance and gait from 459 subjects aged 65 and over, living in Dicomano, a small town near Florence, Italy. Data on fear of and frequency of leaving the house, outdoor activities, and falls in the last month, were used as indicators of a "preclinical" stage of functional decline in mobility. The level of self-reported functional disability was estimated using the WHO scale assessing both activities of daily living (ADL) and instrumental activities of daily living (IADL). Subjects reporting severe disability in ADL were excluded from the analysis, because of the high proportion of data missing in this group. In the subjects not reporting disability as well as in those reporting disability in IADL, indicators of "preclinical" mobility problems were associated with a lower performance in balance and gait. Results suggest that measures of physical performance might detect an early stage of functional decline, when autonomy in ADL/IADL is still intact. Furthermore,in subjects affected by IADL disability, measures of performance provide information which can be used to identify the domain of the functional limitation.

(Ferrucci, Guralnik, Lamponi, Costanzo, Salani, Marchionni, Baroni. *Giorn Geront* 1992;40:227-33.)

- To assess the role of demographic factors and chronic conditions in maintaining mobility in older persons, this study utilized longitudinal data collected as part of the EPESE between 1981 and 1987 on 6,981 men and women aged 65 years and older in East Boston, Massachusetts; Iowa and Washington counties, Iowa; and New Haven, Connecticut. Results were presented for those who at baseline reported intact mobility, defined as the ability to climb stairs and walk a half mile without help, and who were followed annually for up to 4 years for changes in mobility status. Age, income, education, and chronic conditions present at baseline and occurring during follow-up were evaluated for their association with loss of mobility. Over the follow-up were evaluated for their association with loss of mobility. Over the follow-up period, 55.1% of subjects maintained mobility, 36.2% lost mobility, and 8.7% died without evidence of mobility loss prior to death. In both men and women, increasing age and lower income levels were associated with increased risk of losing mobility, even after controlling for the presence of chronic conditions at baseline. After adjustment for age, income, and chronic conditions, lower education levels were a significant risk factor for mobility loss in men, but not in women. Baseline reports of previous heart attack, stroke, high blood pressure, diabetes, dyspnea, and exertional leg pain were associated with small but significant risks for mobility loss. There was a stepwise increase in the risk of mobility loss according to the number of chronic conditions present at baseline that was very consistent between men and women. The occurrence during the study of a new heart attack, stroke, cancer, or hip fracture was associated with substantially greater risk of mobility loss than was associated with the presence of these conditions at baseline. (Guralnik, LaCroix, Abbott, Berkman, Satterfield, Evans, Wallace. *Am J Epidemiol* 1993;137:845-57.)

- Persons of low socioeconomic are known to have reduced life expectancy. In a study of the relation of socioeconomic status to disability-free or active life expectancy among older persons, we analyzed prospectively gathered data on 2,219 blacks and 1,838 whites who were 65 years of age or older in the Piedmont region of North Carolina. We defined disability as the inability to perform independently one or more basic functional activities such as walking, bathing, dressing, eating, and using the toilet. For subgroups defined by sex, race, and education, statistical models were used to estimate, for persons at each year of age, the probability of transition from not being disabled or being disabled at base line to not being disabled, being disabled, or having died one year later. These transition probabilities were then entered into increment-decrement life tables to generate estimates of total, active, and disabled life expectancy (with total life expectancy equal to active life expectancy plus disabled life expectancy). Sixty-five-year-old black men had a lower total life expectancy (11.4 years) and active life expectancy (10 years) than white men (total life expectancy, 12.6 years; active life expectancy, 11.2 years), although the differences were reduced after we controlled for education. The estimates for 65-year-old black women (total life expectancy, 18.7 years; active life expectancy, 15.9 years) were similar to those for white women. Black men and women 75 years old and older had higher values for total life expectancy and active

life expectancy than white, and the differences were larger after stratification for education. Education had a substantially stronger relation to total life expectancy and active life expectancy than did race. At the age of 65, those with 12 or more years of education had an active life expectancy that was 2.4 to 3.9 years longer than the values for those with less education in all the four subgroups defined by sex and race. Overall, the subgroups with longer total life expectancy and active life expectancy also lived more years with a disability. Among older blacks and whites, the level of education, a measure of socioeconomic status, has a greater effect than race on total life expectancy and active life expectancy. (Guralnik, Land, Blazer, Fillenbaum, Branch. *N Engl J Med* 1993;329:110-16.)

- While positive health behaviors have been shown to extend life, their association with extending active life has not been well investigated. Several health behavior were investigated in relation to maintaining mobility during 4 years of follow-up among 6,981 men and women aged 65 years and older with intact mobility at baseline between 1981 and 1983 who lived in one of three communities: East Boston, Massachusetts; Iowa and Washington counties, Iowa; and New Haven, Connecticut. Intact mobility, defined as the ability to climb up and down stairs and walk a half mile, was determined annually by interview, and study subjects were classified into one of three categories at the end of 4 years of follow-up: 1) maintaining mobility (55.1%); 2) lost mobility (36.2%); or 3) died without evidence of having lost mobility prior to death (8.7%). After adjustment for age and all of the health behaviors, risk of losing mobility was significantly associated with current smoking, not consuming alcohol compared with small-to-moderate amounts of alcohol consumption, high (>80th percentile) compared with moderate (21-80th percentiles) body mass index, and low physical activity levels in both men and women. These findings suggest that positive health behaviors can not only extend longevity but also reduce the risk of losing mobility and independence in later life. (LaCroix, Guralnik, Berkman, Wallace Satterfield. *Am J Epidemiol* 1993;137:858-69.)

- Mortality associated with handedness was examined in two ways. A simulation using national data suggests that lower mean age at death among left-handed persons, previously offered as evidence of higher mortality, can be explained exclusively by the age distribution of laterality. Second, empiric evidence from the East Boston EPESE study of 3,774 older adults demonstrates that left-handedness is not associated with mortality (relative odds=1.04% confidence interval=0.79%, 1.39). (Salive, Guralnik, Glynn. *Am J Public Health* 1993;83:265-67.)

- The association of sociodemographic factors was examined with functional blindness and visual impairment in three EPESE sites (East Boston, MA; New Haven, CT; and Iowa and Washington Counties, IA). Persons aged 71 years and older were screened for bilateral functional near and distant vision during an in-home interview in 1988. Screening was completed by 5,335 participants. The prevalence of functional blindness increased with age, from 1% at age 71 to 74 years to 17% in those 90 years of age and older. Functional visual impairment increased from 7% at age 71 to 74 years to 39% in those 90 years of age and older. In multivariate analyses, residence in a nursing home, older age, glaucoma, insulin-

requiring diabetes at baseline, East Boston site, history of cataract, and lower 1982 income were independent and significantly associated with both functional blindness and visual impairment. Age and nursing home residence were significantly ($P<0.05$) more strongly associated with blindness (odds rations 4.8 and 6.1, respectively) than they were with visual impairment. Functional blindness and visual impairment are quite prevalent among the oldest old and the institutionalized. The number of affected individuals will increase as the population ages and life expectancy increases. Although visual problems are associated with aging, nursing home residence, health problems, and socioeconomic conditions, they may be readily remediable and may lead to immediate improvements in quality of life. (Salive, Guralnik, Christen, Glynn, Colsher, Ostfeld. *Ophthalmology*, 1992;99:1840-47.)

- Pneumonia is the fifth leading cause of death among older persons in the United States, and its mortality rate increased over 25 percent between 1982 and 1988. The authors examined the role of functional and cognitive limitations in the risk of pneumonia mortality in older adults. As part of the EPESE study in three communities (East Boston, MA; New Haven, CT; and Iowa and Washington Counties, IA), 6,234 women and 4,035 men aged ≥ 65 years completed baseline interviews between 1981 and 1983 and were followed for up to 6 years. Gender-specific Cox proportional-hazards regression models were used to examine the association of baseline physical and cognitive functioning with report of pneumonia (ICD9 480-486) as an underlying, immediate or contributing cause of death. During followup, a total of 243 men and 160 women died with pneumonia. Adjusting for age, race, education, evidence of 5 chronic diseases, and smoking status, a significantly ($p < 0.05$) increased risk of pneumonia mortality was found for limitations in activities of daily living and cognitive impairment in both men and women. Inability to walk ½ mile, climb stairs or perform heavy housework was significantly associated with increased risk of pneumonia mortality in women but not in men in the same multivariate models. Men and women whose body-mass index was above the median had significantly lower risk of pneumonia mortality compared with those in the lowest quartile. Further elucidation of the sequence between physical and cognitive impairment and risk of pneumonia will be important in reducing pneumonia-associated morbidity and mortality. (Salive, Satterfield, Ostfeld, Wallace, Havlik. *Public Health Rep* 1993;108:314-22.)

- Septicemia is the tenth leading cause of death among older adults in the United States; its mortality rate has steadily increased over the past decades. Little is known about factors which predispose to septicemia mortality in the elderly. The authors investigated risk factors for septicemia-associated mortality in 10,269 older adults as part of the EPESE study in three communities (East Boston, MA; New Haven, CT; and Iowa and Washington Counties, IA). During 6 years of follow-up, 177 persons (3.2 per 1,000 person-years) had septicemia (ICD9 038) reported on their death certificate. In a multivariate proportional-hazards model, septicemia mortality was significantly ($p < 0.05$) and independently associated with age, male gender, history of diabetes, history of cancer requiring hospitalization, smoking one pack of cigarettes/day or more, not drinking alcohol in the year prior to baseline, disability in activities of daily living, cognitive impairment, and missing cognitive testing score. These factors might be useful in developing an at-risk population for testing septicemia treatment or

prevention strategies in a community setting. Further investigation is needed to explain underlying mechanisms of increased risk of subsequent septicemia. (Salive, Wallace, Ostfeld, Satterfield, Havlik. *Public Health Rep*, 1993;108 in press.)

- The association was examined between husband's health and the mental health of community dwelling white women 65 to 75 years of age and how the wife's health, socioeconomic and social resources and marital quality affect this relationship. Husband's health strongly predicts wife's mental health; the negative impact of which is more pronounced when the wife has poor or declining health as well. Marital quality is the strongest predictor of the wives' mental health. Analyses examining the independent and joint effects of marital quality and husband's health on wife's mental health indicate that the negative association of illness in a spouse on wife's mental state is a function of the impact husband health has on marital intimacy and shared pursuits. On the socioeconomic and social substantial relationship to the wife's mental health. (Simonsick EM. *J Aging Health* 1993 in press.)

- It remains unknown whether inactivity not due to disease processes increases risk of morbidity and mortality in older adults. Data from three sites of the EPESE were used to examine the association between recreational physical activity among physically capable older adults and functional status, incidence of selected chronic diseases, and mortality over 3 and 6 years. A high level of recreational physical activity reduced the likelihood of mortality over both 3 and 6 years. A consistent relationship between activity and new myocardial infarction or stroke or the incidence of diabetes or angina was not found after 3 or 6 years. Findings suggest that physical activity offers benefits to physically capable older adults, primarily in reducing the risk of functional decline and mortality. Future work must use more objective and quantifiable measures of activity and assess changes in activity levels over. (Simonsick, Lafferty, Phillips, Mendes de Leon, Kasl, Seeman, Fillenbaum, Herbert. *Am J Public Health*, 1993;83 in press.)

CONTRACT

Name and Number: The Johns Hopkins University School of Medicine (N01-AG-1-2112)

Title: Women's Health and Aging Study

Date Contract Initiated: July 1, 1991

Current Annual Level: $1,877,654

Objectives: The overall goal of the study is to understand the causes and course of physical disability (defined as a deviation or alteration in normal functional performance) in older women living in the community. This will be accomplished by (1) screening a representative population of community-dwelling older women to recruit a study cohort of women with moderate to severe dependence in physical functioning, (2) characterizing prevalent diseases and conditions in members of this cohort and assessing the impact of these conditions on physical function, and (3) following the cohort prospectively for a period of 3 years to evaluate change in functional status.

Methods Employed: Participants in the study are selected at random from among women aged 65 and over living in community residences in 12 zip code areas of Baltimore City and County. The initial sample will include 5,500 women, stratified by age so as to ensure sufficient numbers in the oldest age groups. A brief screening interview will identify approximately 1,270 women who are moderately to severely disabled, defined as being disabled in 2 or more of 4 specified domains of functioning. Of these, about 1,000 are expected to agree to participate in the remainder of the study. These women will complete a baseline interview and an examination conducted in their homes by a nurse practitioner that includes performance-based measures of disability. Follow-up interviews will be conducted with participants every 6 months for the next 3 years.

Significance to Biomedical Research: This study has a number of aspects that make it unique as an epidemiologic study and add substantially to previous work done on disability in older populations. Epidemiologic studies in general have tended to study factors leading to the onset of incident disease, with little study of subjects once disease occurs. This study will examine women who already have disease and disability, attempt to understand the diseases underlying that disability and then prospectively evaluate the course of disability and how the underlying diseases as well as health habits, psychological, cognitive, social and other factors affect that course. Unlike previous epidemiologic research on disability, this study will intensively evaluate diseases and physiologic dysfunction that are associated with disability.

Proposed course: The first 15 months of the study were primarily concerned with planning, development of assessment protocols, creation of an OMB package, and pre-testing of questionnaire and examination instruments. Fieldwork began in November 1992. Baseline assessments, which include an interview, an examination by a nurse, and obtaining a blood

sample, will run through July 1994. Follow-up assessments, which will be done every 6 months for 3 years, began in May. Reports from field supervisors, interviewers, and nurses indicate that the study is being well received by participants, no serious difficulties have been encountered, and screening and recruitment of eligible women into the study has gone well. The use of Computer Assisted Personal Interviewing (CAPI) is a major benefit to the data collection activity, allowing for analysis of data soon after the interview is completed.

The sampling for this study has been designed to stratify the full target population into four replicates, each representative of the entire geographic area. As of July 20, 1993, 823 women from the first replicate have been screened, and 296 (36.0%) have been found to be eligible for the study. Included in these numbers are participants in the "First Fifty Study," composed of a stratified random subsample of 309 women in the first replicate. This cohort of women was created in order to assess the effectiveness of the sampling and screening strategies in identifying and recruiting the projected number of women into the study. Screening in this group is complete and data are currently available for analysis. Overall, study participation is on target. The number of women enrolled in the study from the "First Fifty Study" was expected to be 57, while the actual number is 62. Of those screened, 36% were expected to be disabled in two or more domains of function; in fact, the percentage was 37.6%. The age distribution of study participants is close to that projected, with 38% in each of the 65 to 74 and 75 to 84 year groups, and 25% aged 85 and over. A slightly higher than expected percentage of the sample, which is identified through HCFA records, has been found to be deceased or institutionalized. Refusals are higher than expected at the screener stage, but lower than expected among those eligible for the study after screening. Women in the oldest age group (85 and over) were more likely than younger women to refuse screening, but of those in this age group who were screened, two-thirds were disabled in two or more domains and eligible for the study. The data indicate that the overall yield of the screening process is on target, even though projected estimates for some parameters were higher or lower than what is being encountered in the field. Based on these results, no changes will be made in the screening strategy. The analyses will be repeated when the first replicate is completed to verify the findings.

EDBP staff, working in collaboration with Johns Hopkins investigators and the Westat subcontractor, have played an important role in the developmental and field work for this study, including recent work on the development of the follow-up assessment and the proxy follow-up interviews, to be used when participants are unable to report for themselves and when participants have died. Nurses and interviewers have been trained by EDBP staff to conduct the performance measures of functioning as well as ongoing quality control in this area. EDBP staff facilitated working with HCFA to obtain the Medicare beneficiary files for the study sampling and the Part A and B utilization data for analysis. Staff also coordinated study efforts to obtain readings of the participant spirometry measurements from NIOSH. A Manual of Operations is being prepared to provide an overview of the study and the sources and references for all the data collection instruments and procedures as well as the documentation for all the analytic variables in the study. EDBP staff have also directed the creation of the drug data base for the study.

CONTRACT

Name and Number: University of Iowa (N01-AG-0-2106)

Title: Established Populations for Epidemiologic Studies of the Elderly (EPESE)

Date Contract Initiated: June 30, 1980

Current Annual Level: $328,945

Objectives: The purpose of this project is to conduct epidemiologic investigations in a community to develop new knowledge concerning the medical and social factors in health and diseases of the aged.

Methods Employed: The project includes cross-sectional and prospective studies in a carefully defined and accessible population using standard field and analytical techniques. Yearly surveillance of the population is included.

Significance to Biomedical Research: The population over age 65 has been steadily increasing both in relative and absolute numbers. With this increase has come an awareness of a variety of health and social problems which are creating problems for our social and physical environment. To provide new knowledge, it is important to study representative community-dwelling populations. Within obvious logistical constraints populations will be available to the NIA scientific community for specific studies.

Proposed Course: Continued surveillance during a 5-year period (1989-93) will be based on the use of the National Death Index for mortality and the Health Care Financing Administration's Medicare data for morbidity. While contract closeout will occur this calendar year, intensive research efforts will continue.

Major Findings: Prospective evidence for predictors of decline in social relationships over a 3-year follow-up period in an elderly cohort are presented. The cohort consisted of men (n=903) and women (n=1,673) over age 65 years in two rural Iowa counties who were interviewed in 1982 and again in 1985. Three separate measures of social relationships were dichotomized into lower and higher levels and included the number of close friends and relatives (less than three vs. three or more), church attendance (less than once per month or not at all vs. once per month or more), and membership in a group (nonmember vs. member). Those with higher social relationship levels at both interviews were compared with those who had higher levels at baseline but lower levels at follow-up (i.e., a decline in social relationship level) using logistic regression. In multivariate analysis, important baseline predictors of decline in social relationship levels included greater age, lower education level, lower memory test score, the presence of physical disabilities, and a higher level of depressive symptoms. Marital status and lower self-perceived health status were less consistent predictors, and having any living children, history of major illness, and continence

status were generally not important predictors of decline in social relationship levels. These findings underscore the multifactorial and complex influences on changes in social relationships, but they also identify factors for possible prevention and intervention strategies (ref. 1).

To describe the incidence and health resource consequences of self-reported adverse drug reactions (ADRs) and their relation to self-perceived health, number of medications used, and age in a geographically based population 65 years of age and older. A survey of a defined population. Three thousand, one hundred seventy noninstitutionalized persons 65 years of age and older residing in two Iowa counties. Reports of ADRs (elicited using an open-ended questionnaire); names of drugs involved; descriptions of reactions and related health resource use; self-perceived health status (at the first annual follow-up); and number of medications (from the baseline interview). Ten percent (95% CI, 8.97 to 11.09) of respondents reported one or more ADRs. Three quarters of respondents who reported ADRs contacted a physician. Of these, half indicated that a laboratory test had been ordered, and 7% reported a hospitalization due to the reaction. Advanced age alone was associated with decreased risk in women; a similar trend in men was not statistically significant. However, persons with poorer health status and those who reported the greatest prior use of medications were most likely to report reactions. In this study of noninstitutionalized elderly persons, advanced age did not appear to be associated with increased risk for self-reported ADRs. We could not determine whether the decrease in ADR reports among the oldest respondents represented true diminished ADR occurrence or altered ADR detection and reporting capabilities. When projected to the elderly community-dwelling U.S. population, 2.2 million annual physician visits, 1.1 million laboratory tests, and 146,000 hospitalizations may result from ADRs (ref. 2).

Depressive symptomatology was examined in a large sample of noninstitutionalized older adults using the Center for Epidemiological Studies-Depression scale (CES-D). Both cross-sectional and longitudinal data showed age-related increases in mean CES-D scores and increases in the percent age of respondents scoring at or above the cutoff score of 16. Variables collected at baseline in the longitudinal study from 2,032 participants 65 years of age and older were significant predictors of depressive symptomatology 3 and 6 years later. Baseline CES-D scores accounted for the largest proportion of the variance (ref. 3).

Driving requires the continuous integration of sensory, cognitive, and motor skills, many for which are subject to age and illness-associated impairments. This article reviews functions related to driving, the methods used for their measurement, the epidemiology of age-associated functional impairments, and the relationship of functional impairments to driving behavior and legal interventions. Analyses presented here indicate that although physical functional impairments appear to be associated with both voluntary changes in driving habits and legally imposed regulations, cognitive impairments are associated with legally imposed restrictions but only modest voluntary changes. Suggestions are made for further research aimed at developing reliable and valid screens for functionally impaired drivers and interventions that will maintain or enhance the skills of already impaired drivers (ref. 4).

Publications

1. Cerhan JR, Wallace RB. Predictors of decline in social relationships in the rural elderly. Am J Epidemiol 1993;137:870-80.

2. Chrischilles EA, Segar ET, Wallace RB. Self-reported adverse drug reactions and related resource use: A study of community-dwelling persons 65 years of age and older. Ann Intern Med 1992;117:634-40.

3. Wallace J, O'Hara MW. Increases in depressive symptomatology in the rural elderly: Results from a cross-sectional and longitudinal study. J Abnormal Psychology 1992;101:398-404.

4. Colsher PF, Wallace RB. Geriatric assessment and driver functioning. Clinics in Geriatric Medicine 1993;9(2):356-73.

Asia-Pacific Office

The Asia-Pacific Office (APO) plans and conducts epidemiological studies predominantly among Pacific and Asian populations, and coordinates new international and cross-cultural research aimed at investigating risk factors for dementia, impairments, aging-related diseases, and other concomitants of aging. The Office was established in August 1990, with the assignment of its Chief (Dr. Lon White, formerly Chief of the Epidemiology Office) to Honolulu. The Office is based at Kuakini Medical Center in space provided by that institution through a National Heart, Lung, and Blood Institute (NHLBI) contract in support of the Honolulu Heart Program (HHP). The APO serves as the nucleus of the Asia-Pacific Office for Research on Aging (APORA), an informally constituted and named multi-agency entity currently comprised of representatives from the NIA (Dr. White), the National Center for Nursing Research (NCNR) (Dr. Carolyn Murdaugh -- currently working in the Bethesda office of the NCNR), and the Department of Veteran's Affairs (DVA) (Dr. George Webster Ross). The primary activities of the APORA, as it operates at present, are related to the conduct, direction, and utilization of the Honolulu-Asia Aging Study (HAAS) as a scientific research project.

Honolulu-Asia Aging Study

The HAAS is conducted through a multi-institutional cooperation among personnel of the NIA, the prime contractor (Kuakini Hospital), sub-contractors (University of Hawaii and others), the DVA, NCNR, and the NHLBI. The basic purpose of the HAAS is to utilize the HHP as a resource for research on dementia, and to conduct the study so as to allow comparisons of results with those generated by parallel studies in other populations. The HHP is a longitudinal study of heart disease and stroke that began more than 25 years ago and is directed by the NHLBI through a research contract with the Kuakini Medical Center. The principal scientific goals of the HAAS involve definitions of rates, patterns, correlates, and predictors of cognitive decline, dementia, Alzheimer's disease (AD), and cerebrovascular dementia. In addition, a substantial amount of the research is related to methodological issues, including the development and application of instruments for use in cross-cultural studies, issues related to sensitivity and specificity of methods and instruments in such studies, and validation of diagnoses (to examine endpoint misclassification problems). Funding for the HAAS is accomplished by an interagency agreement between the NIA and the NHLBI to support an aging and dementia supplement to the NHLBI's HHP contract.

Plans are currently being developed for the goals and content of a new cycle of examination to begin in 1994. These will include an expanded role for the National Center for Nursing Research Caregiver Study, a study of body composition and health in a sample of HHP participants having four distinct patterns of weight stability/change over their lifetimes, associations of clinical functioning with structural brain changes on MRI, and bilingual functioning and brain structure in late life of a group of participants who were fully bilingual in middle adult life.

FY93 Accomplishments

About 3,800 of the approximately 4,600 HHP participants have been contacted thus far (4th HHP exam; data as of July 1, 1993), including approximately 3,500 who have received all or almost all of the standard examination and interview. The basic examination (referred to as Module I) will end in September 1993. Approximately 20 to 25 minutes of the Module I examination is devoted to NIA data collection, including administration of the Cognitive Abilities and Screening Instrument (CASI) and a questionnaire to elicit information concerning possible risk factors for dementia. Approximately 13 percent of the examined participants were invited back for a follow-up examination (Module II level 1). Those invited back include all of the participants who receive low CASI scores, about 33 percent of those who received borderline scores (74-82, N=176), and 7 percent of those who received normal (>82, N=165) CASI scores. The purpose of this call-back examination is to carry out a highly standardized dementia evaluation following guidelines previously agreed upon and from which an algorithmic dementia classification can be accomplished with a minimum of subjective interpretation and clinical judgement.

The Module II Level 1 examination consists of a re-administration of the CASI, a test of reaction time, a test of manual dexterity, the Center for Epidemiologic Studies-Depression (CES-D) scale, a brief hearing test, brief vision test, a standardized neurological examination, and an interview with the caregiver -- usually the spouse, occasionally a son, daughter, or other significant person. Participants who still appear to be demented, together with a randomly sampled group of normal participants, receive a third examination (Module II Level 2), intended to yield an independent diagnosis using conventional state-of-the-art clinical methods following the CERAD protocol.

The Module II Level 2 examination consists of a standardized neurological examination, an augmented version of the CERAD neuropsychological test battery, and a medical history interview with the participant and a proxy informant (usually the caregiver). If dementia appears to be present, a CT scan and selected blood studies are ordered. Approximately 128 participants have been tentatively diagnosed as demented, including 60 attributed to Alzheimer's disease, 46 to vascular dementia, 14 to mixed causes, and the remainder to miscellaneous other causes. Low serum levels of vitamin B12 have been noted in 16 participants with dementia, but were thought to contribute to the dementia in only 4 instances. Although the final consensus committee classifications have been completed for 100 persons, the numbers given above are based on the neurologist's opinion.

Based on rough projections from these preliminary data, it is estimated that the prevalence of DSM-III-R diagnosed dementia (all cause) in the responding HHP cohort is between 5 and 6 percent. An additional 2 percent (approximately) appear to have early or mild dementia, but fail to meet all criteria required for DSMIII-R diagnoses. The HHP **cohort ranges in age from 72-92 years, thus being "older" than most American community populations aged 65+**. Our estimated prevalence in this 72-92 year old population corresponds roughly to a prevalence of 4.0-4.5 percent prevalence in a 65+ population, assuming the usual shape of

the age-specific prevalence curve. It is further estimated that 35-45 percent of the cases of dementia in this group will eventually be attributed to AD, while 25-35 percent will be be attributable to vascular dementia, with a vascular/AD ratio of approximately 0.8. These preliminary estimates suggest that the overall prevalence of dementia among HHP participants is somewhate lower than has been reported in most comparably studied European-ancestry populations. Further, the prevalence of AD in this cohort may be substantially lower than has been estimated from other American and European community studies, while the prevalence of vascular dementia may be somewhat greater. These preliminary estimates appear to be roughly midway between published figures from Japan, and published figures from other studies in the United States.

Approximately 40 autopies in HHP participants have been done since the autopsy recruitment effort began. Autopsy and neuropathologic validation of our cases and (thereby) of the methods used to diagnose dementia in the HAAS will be of extreme importance. Collaborative relationships have been established with a neuropathologist at the Armed Forces Institute of Pathology to carry out special studies related to vascular changes in persons with vascular dementia, and in comparison groups.

Preliminary analyses have been carried out that address factors related to HHP participant performance on the CASI, including: (a) **association of CASI scores with education, occupation, years of education in Japan and the U.S., bilinguality, and age**, (b) **association of CASI scores with evidence of prior stroke and/or cardiovascular disease**, (c) **correlates and predictors of transitory poor performance on the CASI**, (d) **associations of CASI scores at exam 4 with performance on a test of olfactory acuity**.

(a) Among participants whose schooling included some years in Japan and some years in Hawaii, it appears that the positive CASI score association with years of schooling was seen for both, but the association was strongest with years of schooling in Hawaii. It is not yet apparent if this reflects some sort of language factor. These results will be presented at the meeting of the American Geriatrics Society in November 1993.

(b) While a definite association of poor performance on the CASI with prior stroke was evident, no association was seen with prior myocardial infarction or prior coronary bypass surgery. An abstract corresponding to this analysis has been accepted for presentation at the November 1993 meeting of the Gerontological Society of America.

(c) A special analysis of transitory false positive CASI scores (failing defined as <74) was undertaken as part of an effort to develop approaches to the study of false positive screening tests for dementia. Among participants whose initial CASI score was 55-74 (corresponding to a mini-mental state score range of about 15-22, about 45 percent improved by at least 8 points, and had a second score >74. In order to gain some appreciation of what factors might be associated with transitory poor CASI performance, 80 such individuals were compared with an approximately equal size group (designated persistent poor performers) whose initial CASI score was also 55-74, but who remained in the poor performance stratum

(<74) with little or no improvement on retesting (improvement <8 points). The persistent poor performers tended to have a stronger history of cognitive and behavioral deterioration over the prior 10 years (based on the IQCODE score), and more problems with social and physical aspects of daily living (based on score on the Dementia Rating Scale of Blessed, administered to the caregiver). These findings supported the expectation that the persistent poor performance group will contain more demented participants than the transitory poor performance group. There was also a statistically significant association between transitory poor performance (CASI) and slightly younger age, a lower prevalence of a history of stroke, slightly higher fasting blood sugar, lower prevalence of diabetes, and higher monthly intake of alcohol. While all of the persistent poor performers have been received for Module II Level 2 examinations, only about 1/3 of the transitory poor performance group have been selected to receive the Module II Level 2 evaluation. We know that about 75 percent of the participants with persistent poor performance are classified as clinically demented at the Level 2 evaluation; numbers are not yet sufficient to estimate the percentage for the transitory poor performance group. The key question, not yet answerable, is: among the persons with transitory poor performance on the CASI, what proportion are clinically demented now, what proportion are in a preclinical phase of dementia, and what proportion have no dementia? We will not be able to address this question until the next wave of examinations has been completed. At this point, however, we have observed that about half of the participants who "failed" the CASI on initial testing, "passed" it when it was administered again 1-3 months later. Given the known high frequency of false positive dementia screening tests, the cautious clinician might consider the simple expedient of repeating the screening test and obtaining a more careful history from a significant other before or instead of embarking on a long and expensive diagnostic work-up for dementia. These analyses will be repeated with larger numbers of study subjects in October; results will be presented at the November 1993 meeting of the Gerontologic Society of America.

(d) A strong association was demonstrated between olfactory acuity (measured by the 14-item Pennsylvania Smell Test) and the CASI; indeed, poor olfactory acuity was second only to low educational attainment in strength of its association with low CASI scores. We are currently trying to determine if the Pennsylvania Smell Test might simply be testing cognitive functioning, rather than true olfactory acuity.

Analytic and Developmental Accomplishments

As summarized by Roses in a presentation at the June 1993 meeting of the American Acadamy of Neurology, it is now clear that the **apolipoprotein E molecule (apoE) plays an important role in the pathogenesis of amyloid deposition in Alzheimer's disease** (AD). It appears that this protein binds to the beta amyloid peptide (BAP), making it less soluble and more likely to accumulate in neuritic plaques and vessel walls. Immunohistochemical staining suggests a similar binding of apoE with an as yet unidentified component of the neurofibrillary tangle (an intra-neuronal lesion of AD). Of the three common isoforms of apoE, epsilon 4 appears to have an especially strong avidity for BAP. Further, the apoE4

allele frequency has been shown to be doubled or tripled among patients with late onset AD (either familial or sporadic), compared with the non-demented population. **Our findings (White, Schellenberg, et al, being prepared for submission) confirm the importance of the epsilon E4 isoform (and the corresponding allele) as an important risk factor for late onset AD.** From our data it appears that the relative prevalence for AD in apoE4 heterozygotes (apoE 4|3 or 4|2) in the HHP cohort now is approximately 2.4, using the most common genotype (apoE 3|3) as the reference group. Our data cannot be used to estimate the relative prevalence of AD associated with the 4|4 homozygote genotype, since there were only 2 homozygotes among the approximately 280 persons typed (one occurring among the 48 cases of AD, the other in a group of 49 cases of Parkinson's disease). Calculations from the HAAS data suggest a population attributable fraction of 21 percent; i.e., if there were no apoE4 positive HAAS participants, it is estimated that the total number of cases in the cohort would be 21 percent less than actually observed. It seems quite possible that apoE type may prove to be the single most important **common** genetic mediator of susceptibility for the development of AD.

The apoE 4 allele frequency appeared marginally elevated in HHP cases of Parkinson's disease. It is not yet clear if the finding is spurious or meaningful.

A major scientific rationale and purpose underlying the establishment of the HAAS was a need to determine the prevalence and incidence of AD in Japanese-Americans. This imperative was based on multiple published reports indicating a lower prevalence in Japan -- apparently 1/3-1/2 that in the US. From the outset it was recognized that these reported differences in prevalence could be entirely spurious (due to methodologic or diagnostic differences), or they could be true and due to genetic factors, environmental factors, or to some combination thereof. Previous genetic studies have established that the frequency of the apoE4 allele varies greatly among different ethnic groups and is low in Japanese (8-11 percent) compared to 13-19 percent for most European-ancestry groups. In the HAAS/HHP population the apoE4 allele frequency appears to be about 10 percent, with prevalence estimates for the 4|4 genotype at 1 percent, and for E4 heterozygosity at 18 percent. In European-ancestry populations, corresponding values are about 2.5 percent (E4 homozygotes) and 27 percent (heterozygotes). Our preliminary calculations suggest that the lower apoE4 allele frequency among Japanese persons could explain some but probably not all all of the reported difference in AD prevalence between Japan and the U.S.

While discordance in fact and age of onset in monozygotic twin pairs (one affected) seems to establish that some exposure/ environment factors must influence the development of AD, case-control studies have been woefully unfruitful in explication. A search for environmental risk factors among the Japanese-American men participating in the HHP will be far more likely to yield meaningful information when we are able to take each participant's apoE type into account, and when we can compare cases with controls of the same age **and from the same apoE genetic susceptibility stratum**. In addition, knowledge of each participant's apoE type will allow us to examine possible relationships between it and age-associated cognitive decline, brain atrophy (by MRI or autopsy), and survival (hypothesis: apoE4

prevalence falls with older age). These analyses will have bearing on the hypothesis that subclinical Alzheimer pathologic mechanisms are responsible for the cognitive declines and atrophy that are commonly attributed to normal aging.

Arrangements are currently being developed to test stored serum or buffy coat samples in order to detemine the apoE4 types of all HHP participants.

The HAAS as a component of the NI-Hon-Sea-Tai Project.

The HAAS evolved as part of a larger plan to develop a series of parallel studies of dementia in Asian-ancestry persons living in different parts of the world. That larger effort, the Ni-Hon-Sea-Tai project, is a coordinated series of epidemiologic studies on dementia that includes: (1) HAAS, (2) the KAME project, a closely coordinated study conducted among Seattle's older Japanese-American population (funded as an NIA grant), (3) a survey in the Adult Health Study Cohort of the Radiation Effects Research Foundation (REFR) (Hiroshima), (4) a survey to be conducted in Kawasaki City (St. Marianna's University and the Tokyo Metropolitan Institute of Gerontology), and (5) surveys to be conducted in Taipei (National Taiwan University and the Veteran's General Hospital). The project was organized by the Asia-Pacific Office and is continued as a shared effort by the cooperating scientists. A central goal is to develop and use methods sufficiently alike so that comparisons of rates and patterns of dementing illnesses across sites will be valid and meaningful.

Close cooperation with the KAME project was continued with frequent telephone communication, by visits of KAME researchers to Honolulu as consultants to the HHP contract, and by continued participation of Dr. White as a member of the KAME scientific advisory committee. Collaboration with Taiwanese researchers was reflected in completion of an initial survey of cognitive functioning and dementia using CASI and other key instruments in Taiwan (Taipei VA hospital group; manuscript in development), by CASI validation studies at the Taiwan National University, and by application of a third Taiwanese group for Taiwan funding of a survey of dementia in urban Taipei. Collaborative research in Hiroshima is ongoing. Research in Kawasaki City and Tokyo is underway. In addition, collaborative relationships were established during this year with researchers at Kyushu University, Hisiyama City, and the National Cardiovascular Center (Osaka) that will allow for comparisons of neuropathologic outcomes using autopsy information and subjects dying in the township of Hisiyama (evaluated with the CASI during the year prior to death) and similar neuropathologic observations in HAAS subjects.

Travel and Presentations

Dr. White convened and chaired a workshop in Honolulu on changes in linguistic competence in bilingual persons during aging and during the development of dementia, October 9-10, 1992.

Dr. White traveled to Washington D.C. to attend the annual meeting of the American Geriatrics Society and the Gerontological Society of America; at those meetings he participated in the meeting of the World Health Association panel for study of age-related dementias; he also presented an overview of the Ni-Hon-Sea Project at a session entitled, "Multi-National Epidemiologic Studies of Dementia" November 14-18, 1992.

Dr. White traveled to Seattle, Washington, March 1-3, 1993, to deliver buffy coat specimens to the laboratory of Dr. Gerard Schellenberg, and to plan a research project related to a possible association of apolipoprotein E genotype with dementing illnesses of late life.

Dr. White spoke at a workshop on dementia, March 19, 1993, organized by the State of Hawaii Executive Office on Aging, together with the Hawaii Chapter of the Alzheimer's Association.

Dr. White attended the annual meeting of the Society for Epidemiologic Research in Keystone, Colorado, June 1993.

Dr. White participated in the NIA Summer Institutes in Research on Aging July 1993, held at the Airlie House in Warrenton, Virginia.

Research Highlight FY93

- We analyzed the association of education, occupation, and sex with incidence of cognitive impairment using data from three communities in the EPESE projects (New Haven, East Boston and Iowa). Participants were initially interviewed in 1981-1983, with followup 3 and 6 years later. Incident cognitive impairment was defined on the basis of either: 1) increase in the number of errors in Short Portable Mental Status Questionnaire (SPMSQ) (i.e. from a baseline level below the cutoff value to score above the cutoff), or 2) inability to respond to interview questions at a follow-up contact (requiring a proxy informant), or 3) death with a recorded diagnosis of a dementing illness. In multiple logistic regression models, the major factors predicting the development of cognitive impairment were advanced age, any errors on baseline SPMSQ, 8 or fewer years of education, and occupation. Education and occupation remained significant predictors after controlling for age, site, sex, stroke, and baseline SPMSQ score. (White, Katzman, Losonczy, Salive, Wallace, Berkman, Taylor, Fillenbaum, Havlik. *J Clin Epidemiol*, 1993 in press.)

PROJECT NUMBER Z01 AG 07040 03 EDBP

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PERIOD COVERED

October 1, 1992 to September 30, 1993

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)

Honolulu Aging Study

PRINCIPLE INVESTIGATOR (List other professional personnel below the Principle Investigator.)

(Name, title, laboratory, and institute affiliation.)

Lon R. White, M.D., M.P.H., Chief, Asia-Pacific Office, EDBP
Richard J. Havlik, M.D., M.P.H., Associate Director, EDBP
Robert Garrison, M.D., Chief, Field Studies Branch, EBP, NHLBI
G. Webster Ross, M.D., Project Neurologist, DVA
Carolyn Murdaugh, Ph.D., Senior Investigator, NCNR

COOPERATING UNITS (if any)

National Heart Lung and Blood Institute (NHLBI)
National Center for Nursing Research (NCNR)
Department of Veterans Affairs (DVA)

LAB/BRANCH

Asia-Pacific Office

SECTION

Epidemiology, Demography, and Biometry Program

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.9	.85	.05

CHECK APPROPRIATE BOX(ES)

X (a) Human subjects — X (b) Human tissues — O (c) Neither

O (a1) Minors

X (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.) The NIA supplements a research project sponsored by the NHLBI and supported through an NHLBI contract with Kuakini Medical Center in Honolulu, Hawaii, to allow for research on aging and dementia among study participants. The Honolulu Heart Program (HHP) is a prospective study of cardiovascular diseases of American men of Japanese ancestry born from 1900 to 1919 and living on the island of Oahu in 1965. This study will focus on aging, with the emphasis on Alzheimer's disease and multi-infarct dementia. About 3,800 of the approximately 4,600 HHP participants have been contacted thus far, including approximately 3,500 who have received all or almost all of the standard examination and interview. Approximately 20 to 25 minutes of the NHLBI examination is devoted to NIA data collection, including administration of the Cognitive Abilities and Screening Instrument (CASI) and a questionnaire to elicit information concerning possible risk factors for dementia. Approximately 13% of the examined participants were invited back for a follow-up examination. Those invited back include all of the participants who receive low CASI scores, about 33% of those who received borderline scores (74-82, N=176), and 7% of those who received normal (>82, N=165) CASI scores. The purpose of this call-back examination is to carry out a highly standardized dementia evaluation following guidelines previously agreed upon and from which an algorithmic dementia classification can be accomplished with a minimum of subjective interpretation and clinical judgement.

Geriatric Epidemiology Office

The Geriatric Epidemiology Office plans and conducts studies and analyses of data in the areas of biomedical, genetic, metabolic, and gerontological issues. The role of this Office within the EDB Program includes developing programs to integrate biomarker research into epidemiology of aging and defining hypotheses and designing projects related to metabolic/nutritional issues, chronic inflammation, and comorbidity as these areas relate to functional outcomes and mortality in older persons.

The Geriatric Epidemiology Office was established in the Epidemiology, Demography, and Biometry Program with the recruitment of an Office Chief, Dr. Tamara Harris, who joined the program in November 1991. Dr. Harris was recruited from the National Center for Health Statistics, where her epidemiologic work focused on nutrition-related risk factors for morbidity and disability in older persons and the component for older persons from the National Health and Nutrition Examination III Survey.

Over the past year, Dr. Harris has planned and organized a major initiative entitled, "Dynamics of Health, Aging and Body Composition (Health ABC)." This is a study of factors responsible for change in health status in healthier older persons and how these changes in health status reflect in changes in body composition and function. This initiative has received Concept Clearance and the proposal was presented to the NIA Contracts Advisory Committee May 20, 1993.

Dr. Harris has also initiated an augmentation to the Cardiovascular Health Study (CHS) involving measurement of body composition by dual x-ray absorptiometry at Bowman Gray School of Medicine and at the University of Pittsburgh. This initiative has received Concept Clearance and was presented to the NIA Contracts Advisory Committee May 20, 1993. We are now awaiting formal approval from the CHS investigators and will then submit an OMB Clearance.

In addition, Dr. Harris has added several additional professional services contracts for methodologic studies dealing with assessment of body composition and has planned a methodologic study to measure glycoxidation products in a variety of body tissues. Negotiations are now underway with Gerontology Research Center (GRC) investigators to obtain specimens from the Baltimore Longitudinal Study on Aging (BLSA) for this project. Dr. Harris has also initiated a project to measure insulin-like growth hormone levels and concomitants in the NHANES III Study in collaboration with investigators from GRC. These projects are summarized below, along with summaries of continuing projects.

1. **FY93 Projects**

a. Assessment of technologies for body composition in older persons:

With Dr. Steven Heymsfield of the Obesity Research Center of the St. Luke's-Roosevelt Hospital Center in New York City, Dr. Harris will be assessing new technologies, including ultrasound, for measurement of body composition in longitudinal studies of older populations. From this work will also develop an assessment of current methodologies, including an exploration of issues related to measurement of body fat and muscle mass.

b. Measurement of bone fragility and muscle mass with dual x-ray absorptiometry:

With Drs. Thomas Beck and Christopher Ruff of Johns Hopkins, and Dr. Anne Looker of the National Center for Health Statistics, Dr. Harris will be assessing the application of computer-driven equations for the calculation of bone fragility from dual x-ray absorptiometry (DEXA) measurements made in the NHANES III in a multi-ethnic population. In addition, Drs. Beck and Ruff will be assessing the utility of the DEXA to measure muscle mass quantitatively in the thigh.

c. Use of toenails to obtain integrated long-term measurement of glycoxidation products in epidemiologic studies:

Glycoxidation products, such as pentosidine, may be important as indicators of long-term protein changes related to cumulative exposure to hyperglycemia. Currently, there are short term measurements of these products from blood; the only long-term products are in skin, which is impractical for larger scale epidemiologic studies. We initiated a project which is to be carried out in collaboration with investigators in the Baltimore Longitudinal Study on Aging to assess the utility of toenail clippings to obtain a measure of glycoxidation exposure which would integrate 6-12 months of exposure.

d. Measurement of insulin-like growth factor 1 in the NHANES III population:

A proposal to measure insulin-like growth factor 1 in selected subpopulations in the NHANES III population using excess sera was approved pending additional methodologic studies. Dr. Harris is meeting with investigators at the GRC to initiate a collaborative study which would examine whether the cross-sectional age-related decline seen in the BLSA population can be replicated in three ethnic subpopulations: White, African-Americans and Hispanics and to compare the concomitants of levels of IGF-1 in terms of health status and body composition across groups.

2. Updates of Projects Begun in FY92

a. Assessment of the relation of chronic disease burden, weight loss and immune activation:

Data collection in Framingham is two-thirds complete. The measurement of cytokine levels in mononuclear cells at Tufts, levels of inflammatory proteins and associated other biochemistries has been successful. Methodologic work over the year suggests that the delay of an hour in laboratory processing while the specimens are being transported from Framingham to Tufts has some effect on the measurements but that data from healthy younger persons in Framingham should allow some adjustment. Preliminary data on both stimulated and unstimulated levels of IL-1, TNF and IL-6 shows fairly normal distributions of secretors and non-secretors for each cytokine. Preliminary analyses are ongoing and data collection should be complete this fall.

b. Determinants of Healthy Aging:

Dr. Harris has continued to work with Dr. Stefania Maggi of the Special Program for Research on Aging of WHO. In addition to the meeting last September to assess measures of physical performance, there was a consultation session in which blood and other physical measurements were discussed. Dr. Gary Andrews is in the process of preparing a protocol for the pilot tests which will take place in Costa Rica, Italy and Thailand.

c. WHO Anthropometry:

Dr. Lenore Launer and Dr. Harris prepared background data on distributions of height, weight, and body mass index and variation with age and health status for selected populations of older persons. These data were presented to the Steering Committee meeting in October 1992 chaired by Dr. Phyllis Eveleth and were incorporated into the report of the committee. In addition, Drs. Launer and Harris are preparing a manuscript for submission summarizing these data.

d. Measurement of insulin-like growth factor in cycle 22 of the Framingham Heart Study:

Data has been transmitted from the Endocrine Sciences Laboratory for approximately 445 specimens. These data are being linked to longitudinal data from the Framingham Heart Study for analysis. Data collection should be completed in November and preliminary analyses will be performed prior to that time.

e. Longitudinal change in cholesterol and HDL in relation to inflammatory proteins:

In several cross-sectional studies, total cholesterol tends to decline with age while HDL levels tend to remain constant. To investigate this in a longitudinal study, a contract was initiated with the Cardiovascular Health Study site at Bowman Gray School of Medicine. This study was delayed by negotiations with a sub-contractor at the University of Vermont, however, blood analyses are ongoing.

f. Study of longitudinal weight change in rhesus monkeys:

A contract was initiated with the manager of a colony of free-living freely-feeding rhesus monkeys maintained on Morgan Island as a breeding colony by the FDA. Data collection is ongoing and we expect to receive a data set soon for analysis.

3. Consultation, Collaboration and Other Professional Activities

Dr. Tamara Harris

Office of Prevention: Dr. Harris participated in site visits for the Women's Health Initiative (WHI). Dr. Harris continues to be involved in the WHI serving as a member of the Observational Cohort Study subcommittee and a member of the Calcium and Vitamin D subcommittee.

WHO Subcommittee on Anthropometry in Older Persons: Dr. Harris continues to participate as a member of this committee; Dr. Eveleth is expected to submit the final report this fall.

Nutrition Office: Attended meetings; assisted in the planning of meeting on Failure to Thrive sponsored by the Geriatrics Program; with Dr. Sam Korper, met with representatives of the Nutrition Screening Initiative and spoke at meeting in May.

NIH Nutrition Coordinating Committee: Alternate representative.

NIA Advisory Committee for the Recruitment of Minorities and Women (ACRMW).

Cardiovascular Health Study (CHS): Dr. Harris has continued to attend the Steering Committee meetings when they occur in Washington. She was asked to participate as a co-author on several CHS publication, particularly those dealing with disability and weight. Dr. Harris has designed a component to assess body composition as an augmentation to the CHS. In addition, she has been working with Dr. Korper, Dr. Richard Suzman and Dr. David Willis to investigate studies of cost of illness which could be performed with the data from the CHS.

Qualifications Review Board (QRB) for NIA: Dr. Harris participated in the evaluation of candidates for a position with Dr. Korper.

USDA Human Nutrition Center on Aging: Dr. Harris continues to work as a member of the Planning Committee for the Bristol-Myers Conference on Nutrition Assessment in the Elderly.

National Cancer Institute: AARP Dietary Survey - Cohort study of several hundred thousand persons age 50 to 69 for dietary factors in cancer incidence.

National Osteoporosis Data Group: Dr. Harris was invited to represent the epidemiologic interests of NIA in a working group convened by the NIAMS.

Weight history working group: Dr. Harris continues with meet with investigators from the National Cancer Institute, the National Center for Health Statistics and the National Heart Lung and Blood Institute to evaluate strategies for obtaining life weight history.

Weight loss conference: Dr. Harris continues to meet with Drs. Diane Bild and Millicent Higgins from the NHLBI to discuss a workshop to evaluate why weight loss appears to increase risk of cardiovascular mortality.

Dehydration working group: Dr. Harris organized a working group to carry out analyses of data on dehydration including members from the Epidemiology, Demography and Biometry group at NIA, the Health Care Research Administration, and the National Center for Health Statistics. One manuscript is close to completion and at least two others are planned.

National Center for Health Statistics:

International Collaborative Effort on Aging: Dr. Harris continues to meet with Dr. Edward Bacon and Dr. Anne Looker from the National Center for Health Statistics and Dr. Stefania Maggi of the WHO Program to complete a second manuscript comparing international rates of hip fractures. The first manuscript appeared in the American Journal of Public Health this year.

National Health and Nutrition and Examination Survey III: Dr. Harris continues to advise regarding the component for older persons and to participate in training of health technicians who are involved in assessment of physical and cognitive function. Dr. Harris is also involved in the planning and augmentation of followup of the NHANES III cohort, evaluation of nonresponse of older persons and beginning analytic projects.

Health Care Financing Administration (HCFA): Technical Advisory Panel for the Post-hospitalization Outcomes Study.

Dr. Harris served as a manuscript reviewer for the following journals: The New England Journal of Medicine, Journal of the American Geriatrics Society, Journal of Gerontology, American Journal of Epidemiology, and the Journal on Aging.

Dr. Harris was invited to become an Associate Editor of the Journal of the American Geriatrics Society.

Dr. Harris reviewed abstracts for the American Geriatrics Society and coordinated the Health Services Research abstract review. Dr. Harris continued her participation as a member of the Research Committee and served as a member of the Task Force on Women for the American Geriatrics Society. She chaired paper sessions at both the American Geriatrics Society and the Gerontological Society of America meetings.

Dr. Harris participated in a workshop in Boston organized by Drs. Guralnik, Winograd and Studenski on performance measures in studies of function.

Dr. Harris, with Dr. Paula Davis of the University of Pittsburgh and Dr. Walter Ettinger of Bowman Gray School of Medicine, organized a small working group to evaluate uses and methods of cytokine measurement in epidemiologic studies.

Dr. Jean Langlois

Centre for Ageing Studies, Flinders University, South Australia: Invited member of the Centre's collaborative research group; involved in questionnaire design and analysis of data from the Australian Longitudinal Study of Ageing.

Center for Injury Prevention and Control, Centers for Disease Control and Prevention: Member of the Study to Assess Falls Among the Elderly (SAFE) Working Group; involved in study design and analysis of data from the SAFE case-control study of risk factors for falls resulting in injury.

National Center for Health Statistics International Collaborative Effort (ICE) on Injury Prevention: NIA representative to this committee working to standardize the reporting of injury deaths and hospitalizations internationally.

National Injury Surveillance Unit (NISU) of Australia: Invited participant in the NISU-sponsored International Injury Colloquium; involved in planning for the 3rd World Injury Conference and the injury research agenda for Australia.

Injury Prevention Research Unit of New Zealand: Consultant on plans for a longitudinal study of risk factors for assault.

Women's Health Initiative Community Prevention Study Working Group: NIA co-representative.

Manuscript reviewer for Public Health Reports.

4. Analytic Efforts

Dr. Harris

Established Populations for Epidemiologic Studies of the Elderly (EPESE):

Body mass index and risk of mortality: with Ms. Kathy Losonczy and Dr. Eleanor Simonsick; abstract for the Society for Epidemiologic Research (SER).

Cholesterol, HDL cholesterol, weight and weight change in older persons: Analysis with Drs. Lori Brown, Marcel Salive, and Robert Wallace (Iowa EPESE PI); data suggests that weight loss is associated with lower levels of cholesterol; low weight is associated with higher HDL levels. However, those with low weight who had experienced significant weight loss who had lower cholesterol and higher HDL levels were in poorer health. Further analysis will explore this paradox and attempt to examine causative factors.

Depression and cholesterol with Dr. Brown.

NHANES I Epidemiologic Followup Study (NHEFS):

Manuscripts submitted for publication:

Weight, weight change and comorbidity as risk factors for disability. Overweight doubles the risk of incident disability in middle aged and older women. In older women even controlling for health conditions, weight loss is a risk factor for disability as well.

Weight and well-being in younger women.

Manuscripts in preparation (from various datasets):

Patterns of weight, height and anthropometric measures from the CHS. This analysis, with Dr. Peter Savage and other investigators from the CHS will document patterns of anthropometric measures and weight change in older persons.

Correlates of weight, height and anthropometric measures from the CHS. This companion manuscript, in which Dr. Harris has lead responsibility, will investigate the correlates of patterns of weight, waist girth and weight change in an older population.

Is proteinuria on dipstick urine a reasonable screening test for significant health problems?

Losing weight and gaining risk. An analysis of weight, weight change and risk of coronary heart disease.

Body mass index and hip fracture--does weight loss increase risk of hip fracture? A comparative analysis is being performed in the EPESE.

Longitudinal Study on Aging: Can difficulty with walking distance and climbing steps be considered to be a state of preclinical disability? Julie Weeks of the National Center for Health Statistics is examining the long term consequences of impairment in higher level function in those free of ADL limitations. Eleanor Simonsick is a member of this analytic project.

Dr. Langlois

Study to Assess Falls Among the Elderly (SAFE) - In collaboration with members of the SAFE working group at the Centers for Disease Control and faculty at the Johns Hopkins Injury Prevention Center, Dr. Langlois is completing work on two studies:

a. A case-control study of the relationship between ADL dependence and the risk of falls resulting in injury: The findings suggest that the estimated risk of an injurious fall is greater among younger elderly people (aged 65-79) with dependence in ADLs as compared with the older elderly, including those with dependence in ADLs and those without. This paper has been submitted to the Journal of the American Geriatrics Society.

b. A case-control investigation of body mass index and its relationship to risk of hip fracture: Dr. Suzanne Smith of the Centers for Disease Control is the first author.

NCHS Mortality Data and New Zealand Health Information Service Mortality Data - Dr. Langlois is currently completing two papers comparing injury death rates among people 65 and older in New Zealand and the United States:

a. Fall injury death rates: The substantially higher injury death rates reported for older New Zealanders can be explained by more complete and accurate classification of fall injury deaths as the underlying cause in New Zealand. These findings reinforce the need for improvements in the management of U.S. mortality data, suggest ways of facilitating those improvements, and emphasize the need for caution in comparing injury death rates cross-nationally. This paper has been submitted to the American Journal of Public Health.

b. Homicide and suicide rates: The greater proportion of firearm-related homicide deaths among older Americans is largely responsible for an overall U.S. homicide rate that is three times the rate for older New Zealanders. Despite a greater proportion of firearm-related

suicides in the U.S., the overall suicide rates were similar for older people in the two countries. These findings suggest that current firearm restrictions in New Zealand may contribute to a lower homicide rate but appear to have little impact on suicide rates among the elderly. Further comparison of New Zealand rates with those for a single U.S. state (Colorado) are currently being conducted.

Uniform Hospital Discharge Data System (UHDDS) Injury Data - Dr. Langlois is continuing her collaboration with the Office of Health Statistics, Rhode Island Department of Health, to complete the research project that she recently directed.

a. Cause of injury coding for hospitalized injuries: Lack of information in the medical record on the cause of injury is frequently mentioned as an impediment to the use of International Classification of Diseases (ICD) cause of injury codes (E-codes), limiting the potential of UHDDS data for surveillance of nonfatal injuries. E-coding rates are particularly low for hospitalized injuries to people 65 and older. In this study, a sample of injury discharges were selected, medical records abstracted, and E-codes assigned based on cause of injury information available in the charts. For 65 to 70 percent of hospitalized injuries with no E-code or a vague E-code reported on UHDDS, a specific E-code could be assigned. Certain forms (e.g., discharge summaries) were more likely than others to supply detailed cause of injury information. The results of this study will be used to support current national efforts to require mandatory E-coding of injuries on UHDDS. Analysis is nearly completed and the final report and manuscript for publication are being prepared.

National Mortality Followback Survey - Dr. Langlois is currently working with faculty and staff at the Johns Hopkins Injury Prevention Center to develop plans for a study examining the co-morbid conditions and medical complications leading to death following injury in people aged 65 and older.

Established Populations for Epidemiologic Studies of the Elderly (EPESE) - In collaboration with Dr. Harris, Dr. Langlois is examining the association between weight history and risk of hip fracture.

Study of Quality of Life of the Elderly in Veneto, Italy - Dr. Langlois is working with Dr. Harris and Dr. Stefania Maggi of the World Health Organization on two analyses: 1) predictors of high level functioning and 2) the epidemiology of hearing impairment and its relationship to quality of life.

Dr. Sorkin

Longitudinal change in height with age - Using data from the Baltimore Longitudinal Study on Aging, Drs. Sorkin, Andres and Mr. Dennis Muller have examined longitudinal change in height with age.

Predictors of wasting syndrome in HIV-1 infected users of indictable drugs - An exploration of predictors of wasting syndrome in users of indictable drugs seropositive for the HIV-1 virus is currently underway. In addition to Dr. Sorkin collaborators in the project include Drs. Paul Bolton, Pornchai Sithisarankul, David Valhov and Neil Graham.

Recommendations for weight for height - Continuing his collaboration with Dr. Reubin Andres and Mr. Denis Muller, Dr. Sorkin has continued to explore current recommendations regarding weight for height. The results of this collaboration has been accepted for publication in the Annals of Internal Medicine.

Coronary heart disease - Working with Dr. Leslie Katzel, Dr. Sorkin has explored risk factors for silent coronary ischemia (SI) in older men. The identification of risk factors is the first step to developing programs which may prevent the development of SI, an early form of coronary heart disease.

Alkylation status and age - In conjunction with Dr. Robert Vestal, Dr. Sorkin has examined cross-sectional differences in alkylation status with age.

Glucose metabolism and health - In conjunction with Drs. Cherry-Peppers, Ship and Baum from the Dental Institute and Dr. Andres from the Gerontology Research Center, Dr. Sorkin has studied the relationship between salivary gland function and the ability to metabolize glucose. The results of these studies have been published in the Journal of Gerontology: Medical Sciences.

5. Talks and Presentations

Dr. Harris

October 1992, invited presentation, Geriatrics Rounds, Johns Hopkins School of Medicine, "Age and Change: Who among the old is at risk?"

October 1992, invited presentation, WHO Committee on Anthropometry, Subcommittee for the Elderly, "International comparisons of body weight and height in older persons."

November 1992, paper presentation, American Geriatrics Society, "Weight loss and risk of hip fracture in postmenopausal white women age 60-74. The NHANES I Epidemiologic Followup Study."

November 1992, invited presentation, Pre-conference data users symposium, "NHANES III: Future expectations."

November 1992, paper presentation, Gerontological Society of America, "Something old, something new: the impact of the past on predicting frailty."

January 1993, invited presentation, NIA Brown Bag Series, "NHANES III: Importance of the survey for older Americans."

February 1993, invited presentation, Mason F. Lord Memorial Lecture, Johns Hopkins University Geriatrics Symposium: Nutrition and Aging, "Is health status the main determinant of nutritional status in old age?"

March 1993, invited presentation, NIH Epidemiology Group, "The ups and downs of low cholesterol."

May 1993, poster, American Federation for Clinical Research, "Weight, weight change and mobility disability in older women."

July 1993, NIA Summer Institute in Research on Aging.

September 1993, Age-related hormonal influences on obesity at NIDDK Workshop: "Prevention of Obesity: Populations at Risk, Etiologic Factors and Intervention Strategies."

Dr. Sorkin

Sorkin JD, Katzel LI, Busby MJ, Lakatta L, Fleg JL. Metabolic risk factors for exercise induced silent myocardial ischemia in apparently healthy men. 65 Scientific Session, American Heart Association New Orleans, Louisiana, November 16-19 1992. (In Circulation Oct 1992, 86(4) Part 2.)

Breslow R, Sorkin J. One day calorie counts: Valid for hospital patients. Annual meeting of the American Dietetic Association, Washington, D.C. 1992. (In J Am Diet Assoc 1992, 92(Suppl):A-91.)

Korrapati MR, Loi CM, Sorkin JD, Vesell ES, Andres R, Vestal RE. Acyelator phenotype in relation to age and gender in the Baltimore Longitudinal Study of Aging. Poster 89 P2 American Society for Clinical Pharmacology and Therapeutics, Honolulu, March 1993. (In Clinical Pharmacology and Therapeutics Feb 1993 p 192.)

Ben Hurley BF, Redmond BA, Smith MM, Smith AS, Rubin MA, Miller JP, Pratley RE, Hagberg JM, Sorkin JD, Goldberg AP. Effects of strength training on muscle hypertrophy and muscle cell disruption in older men. American Society Sports Medicine Meeting Seattle, June 1993. (In Medicine and Science in Sports and Exercise 1993, 25:s149.)

4. Training and Conference Attendance

Dr. Langlois attended the Geriatric Medicine Training Program at Harvard University March 1993.

Dr. Langlois participated in the 2nd World Injury Conference, Atlanta, Georgia, April 1993.

5. New Staff

Dr. Jean Langlois joined the Geriatric Epidemiology Office as an Epidemiologist in February 1993. Dr. Langlois has a Master of Science degree and clinical experience in speech-language pathology, with an emphasis on rehabilitation following closed head injury. She also holds Master's and Doctor of Science degrees from the Johns Hopkins School of Public Health. Her previous research has been largely in the area of injury epidemiology and prevention. At NIA, she will extend her research focus to include both communication disorders and comorbidity, including its relationship to disability and injury risk and outcome. Dr. Langlois came to NIA from the Rhode Island Department of Health where she served as a consultant after completing post-doctoral research fellowships at the University of Otago in New Zealand and Monash University in Australia.

Dr. Lenore Launer, an epidemiologist from the Free University, Amsterdam, The Netherlands, spent the month of September as a Guest Researcher in the Geriatric Epidemiology Office. During this visit Dr. Launer performed analyses of data on cognitive impairment and dementia from the Honolulu Dementia Study with a focus on physical activity, glucose, and lipids.

Dr. Marian A. Parrott, a Clinical Associate Professor at The George Washington University Medical Center in the Division of Aging Studies and Services, Department of Health Care Sciences, arranged a temporary assignment under the provisions of the Intergovernmental Personnel Act (IPA). She will analyze data from the NHANES I Epidemiologic Followup Study with regard to risk factors for prostatic hypertrophy.

John Sorkin, M.D. joined the staff as an Epidemiology Staff Fellow through the PHS Epidemiology Training Program in FY92. Previously he was a Fellow in the GRC's Laboratory of Clinical Physiology. Dr. Sorkin completed a year of academic study in epidemiology at The Johns Hopkins University School of Hygiene and Public Health and the following 2 years will be spent performing research in the EDB Program.

Research Highlights FY93

- The effects of long-term change in body weight on all-cause mortality was analyzed using published studies. Data sources included 13 reports from 11 diverse population studies, 7 from the United States and 4 from Europe. All studies included a weight change period of 4 or more years, followed by a mortality assessment period of 8 or more years. All weight changes occurred in persons 17 years or older. Data from individual studies are presented as number of participants, number of deaths, ages at initial and final weight measurements, duration of the mortality follow-up period, consideration of cigarette smoking and other potential confounders, exclusion criteria, temporal separation between the weight change and mortality follow-up periods, and association between weight change and all-cause mortality. Results were summarized by weight change associated with the lowest mortality rate and by the effects of long-term weight loss on mortality rate. The study concluded that despite the diversity of the populations studied, the degree of "clinical clean-up" at entry, the techniques used to assess weight change, and the differences in analytic techniques (including consideration of potentially confounding variables), certain conclusions may be drawn. Evidence suggests that the highest mortality rates occur in adults who either have lost weight or have gained excessive weight. The lowest mortality rates are generally associated with modest weight gains. (Andres, Muller, Sorkin. *Ann Intern Med*, 1993;118 in press.)

- To determine whether a one-day calorie count can replace the labor-intensive three-day calorie count commonly performed in hospitalized patients when estimates of caloric and protein intake are required. Pilot study using prospective, non-concurrent review of medical records. Hospital. Thirty patients (mean age 67 years). Mean three day intake (952$\pm$91 calories, 41$\pm$4 g protein) was about half of calculated requirements; first-day intake was similar (918$\pm$116 calories, 40$\pm$5 g protein). The first day had high sensitivity (calories: 96%; protein 93%) and positive predictive value (calories: 100%; protein 96%). Malnutrition was evident; three-fourths of patients had weights below recommended ranges and 83 percent were hypoalbuminemic. Three day calorie counts are frequently performed in patients suspected of eating poorly. Results of this pilot study suggest that one day calorie counts may be a valid alternative. However, readily available anthropometric and biochemical data may be as good an indicator of inadequate dietary intake. (Breslow, Sorkin. *J Am Geriatr Soc* 1993 in press.)

- Evaluation of disability is central to assessment and rehabilitation of elderly people, but it is just one component of the disease, impairment, disability, handicap model. In this study, we determined the prevalence of disability in a total community population of people 70 years and over in Mosgiel, New Zealand. We also re-examined the most disabled subjects to determine the underlying diseases and impairments associated with their disability, the social handicap associated with the disability and its relationship to social situation and support. Among the 76 most disabled subjects, the majority had multiple impairments both in the physiological systems assessed (eg. cognitive, sensory) and the integrated functions necessary for dressing. The major diseases associated with disability were heart failure, osteoarthritis,

dementia, stroke and diseases leading to blindness or deafness. The overall odds ratio for being handicapped in subjects with any disability compared to subjects with no disability was 6.65 (95% CI 4.73-9.36). When social support was considered, the estimated risk of handicap associated with any disability ranged from 3.19 (93% CI 1.92-5.30) for participants with a spouse, to 52.0 (95% CI 4.03-670.60) for subjects without emotional support. (Campbell, Busby, Robertson, Lum, Langlois, Morgan. *Disability and Rehabilitation*, 1993 in press.)

- To study the relationship between glucose metabolic status and salivary gland function in different-age persons, subjects with diabetes mellitus (DM=11), impaired glucose tolerance (IGT=26), and controls (n=26), aged 24 to 93, were examined in the oral physiology component of the BLSA. All were generally healthy (except DM) and nonmedicated. The controls and subjects with IGT were classified using World Health Organization criteria, and diabetic status was assessed using HblAc levels. Unstimulated and 2% citrate-stimulated parotid and submandibular salivary flow rates were collected, and subjective responses to questions about salivary hypofunction were evaluated. No statistically significant differences were observed between the three groups, nor between young and old subjects with altered glucose metabolism. These fundings suggest that among well-controlled individuals with altered glucose metabolism, salivary gland function is not significantly impaired. (Cherry-Peppers, Sorkin, Andres, Baum, Ship. *J Gerontol*, 1992;47:M130-M134.)

- Little is known about the relation of overweight of coronary heart disease in older women. In this paper, the authors used measured weight for 1,259 white women age 65-74 years from the Epidemiologic Follow-up Study of the First National Health and Nutrition Examination Survey to examine the effect of overweight on coronary heart disease incidence (mean length of follow-up, 14 years). They also used reported lifetime maximum weight to examine the effect of weight loss on this association. Women with a Quetelet index (weight (kg)/height $(m)^2$) of 29 or more showed an increased risk of coronary heart disease (relative risk (RR)-1.5, 95% confidence Interval (CI) 1.1-2.1) after adjustment for age and smoking in comparison with those with a Quetelet index of less than 21, while women with a Queletet index of 23-24 had a lower risk of coronary heart disease (RR=0.6, 95% CI 0.4-0.9). However, the pattern of risk associated with measured weight was modified by weight loss. Among heavier women whose weight was relatively stable, those with a Quetelet index of 29 or more had an increased risk of heart disease (RR=2.7, 95% CI 1.7-4.4)). Among those with greater weight loss, the relation between Quetelet index and risk of coronary heart disease was J-shaped. Overweight is an independent risk factor for coronary heart disease in older women, a finding strengthened after previous weight loss is accounted for. Reasons for the unexpected increase in risk of coronary heart disease in thinner women who lost weight are unclear and further investigation is warranted. (Harris, Ballard-Barbasch, Madans, Makuc, Feldman. *Am J Epidemiol* 1993;137.)

- Trends were examined by age and sex, with separate statistics for those aged 85 or older. Hospital discharge data were used to obtain hip fracture incidence in Hong Kong and the United States from 1988 through 1989. Within each population, women had higher hip

fracture rates than men. Fracture rates in the United States were significantly higher for both sexes than rates in Hong Kong. For persons over the age of 80, rates of hip fracture among white U.S. males exceeded those for Hong Kong women. Inclusion of transferred cases in hip fracture rates minimized differences between the countries. Despite increasing hip fracture rates in hong Kong, those rates are still substantially lower than the rates in the United States. Identifying factors responsible for this variation may prove useful in the search for preventive strategies. (Ho, Bacon, Harris, Looker, Maggi. *Am J Public Health* 1992;83:694-97.)

- To address the relationships between weight and mortality and weight and disability in old age, data on women aged 70 or older were compared from two studies of health in old age: One from the United States and one from Hong Kong. The mean periods of followup are 32 months and 37 months respectively. In order to eliminate confounding by smoking, the data sets were restricted to elderly women who were never smokers. Proportional hazards analysis shows an inverse relationship between age-adjusted mortality and body mass index (kg/m^2) in both elderly populations. Similar findings were observed after controlling for health and social conditions, and also after excluding subjects with disability at baseline. Disability at baseline and at followup was also highest among subjects belonging to the body mass index group less than 20.36 (kg/m^2) and the findings were consistent in both populations. (Ho, Harris, Madans, Feldman. *Age & Nutrition* 1993;4:88-93.)

- The relation of age to 5-year relative survival rates was examined for leading sites of cancer resulting in death among 127,554 patients; data from 1978 to 1982 were studied for 4 areas of the Surveillance, Epidemiologic and End Results program of the NCI. Overall and stage-stratified relative survival rates declined with advancing patient age for cancer of the lung, prostate, pancreas, bladder, oral cavity, uterus, cervix, ovary, and large bowel (women only). In men, this trend was not explained by age differences in stage of diagnosis , whereas, among women, age was associated with more advanced disease for most sites examined. Although overall survival rates were lower in black patients compared with white patients, the age-survival and age-stage trends were similar in the two racial groups. (Kant, Glover, Horm, Schatzkin, Harris. *Cancer* 1992;70:2734-40.)

- We examined the relation of dietary diversity to subsequent all-cause mortality by using data from the first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study, 1982-1987. The analytic cohort consisted of 4,160 men and 6,264 women (including 2,556 deaths), 25-74 y at baseline (1971-1975). Twenty-four-hour dietary recalls were evaluated for variety among the 5 major foods groups: dairy, meat, grain, fruit, and vegetable, with a dietary diversity score (DDs); consumption of each food group contributed one point to a maximum possible DDS of 5. Age-adjusted risk of mortality was inversely related to DDS ($P \leq 0.0009$) in men and women. The inverse diversity-mortality association was adjusted for potential confounders: education, race, smoking status, and dietary fiber intake; the relative risk of mortality in men and women consuming 2 or fewer food groups was 1.5 (95% CI 1.2-1.8) and 1.4 (95% CI 1.1-1.9), respectively. In conclusion, diets that omitted several food groups were associated with an

increased risk of mortality. (Kant, Schatzkin, Harris, Ziegler, Block. *Am J Clin Nutr* 1993;57:434-40.)

- Increasing parity or gravidity may be risk factors for coronary heart disease; a long debate over this questions remains unresolved. We tested the association between gravity and a variety of cardiovascular endpoints in 2,357 women who were followed for 28 years through the Framingham Heart Study and in 2,533 women followed for a minimum of 12 years through the NHANES I Epidemologic Follow-up Study (NHEFS). All women included in the present study had completed childbearing at baseline. Incidence rates of coronary heart disease, cerebrovascular disease, congestive heart failure, and total cardiovascular disease increased slightly with increasing gravidity in the Framingham Heart Study. Similar increases in coronary heart disease with increasing gravidity were observed in NHEFS women. A continuous variable for gravidity was associated with 4-6% increased rates of coronary heart disease per pregnancy in both Framingham and NHEFS, and with total cardiovascular disease in Framingham, independent of a variety of known cardiovascular risk factors, including weight. Categorical models showed these higher rates to be confined to mutilgravid women and to particularly affect those with 6 or more pregnancies versus no pregnancies (Framingham rate ratio 1.7, 95% confidence interval 1.2, 2.4; NHEFS rate ration 1.3, 95% confidence interval 1.0, 1.8). The association was strongest in multigravid women aged 46-64 from the NHEFS (rate ratio 1.9, 95% confidence interval 1.1, 3.3). Increased gravidity is associated with a small but consistent increased risk for coronary heart disease and cardiovascular disease. This association suggests a variety of potential mechanisms of cardiovascular disease in women. (Ness, Harris, Cobb, Flegal, Kelsey, Balanger, Stunkard, D'Agostino. *N Engl J Med* 1993;328:1528-33.)

- The effect of weight on mortality was examined using data from the first National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study for white women aged 65 to 74 years at baseline. There was a U-shaped curve relating the Quetelet index categories to total mortality, with increased risk for both lean and heavy women. However, the increased risk to lean subjects occurred only among those who had lost more than 8.55% from their reported lifetime maximum weight. Controlling for baseline medical conditions, excluding early years of follow-up, and limiting the analysis to never-smokers did not greatly change the results. Lean women with stable weight have the lowest risk of mortality, while those who have lost weight have a high risk. Heavy women have a high risk of mortality regardless of weight-loss history. Thus, the effect of weight on mortality is modified by history of weight loss in older women, even when accounting for factors associated with weight loss and increased mortality risk. (Rumpel, Harris, Madans. *Ann Epidemiol* 1993;3:343-50.)

- The authors followed 775 men (aged 18-98 years) participating in the BLSA for an average of 10 years. Resting metabolic rate (RMR) and fasting respiratory exchange ratio (RER) were measure by indirect calorimetry on their first visit and related to subsequent weight change. Deviations from the predicted value of resting metabolic rates (predicted from their estimates fat-free mass) were calculated. Average weight change was 0.07 kg

(s.d. 6.4 kg); 122 men (15.3%) gained more than 5 kg and 40 (5.2%) more than 10 kg during the follow-up. After adjustment for initial age, body mass index, fat-free mass, and duration of follow-up, RER, but not RMR or deviations from predicted RMR, was positively related to weight change ($P<0.001$). Major weight gain (from at least 5 kg to at least 15 kg) was related to initial RER in non-obese men only (initial body mass index <25 kg/m^2). From Cox proportional hazard regression analyses the adjusted relative risk of gaining 5 kg or more in initially non-obese men with a fasting RER of 0.85 or more was calculated to be 2.42 (95% confidence interval: 1.10-5.32) compared to men with a fasting RER less than 0.76. It was concluded that a relatively high fasting RER is a weak but significant predictor of substantial weight gain in non-obese white men. (Seidell, Muller, Sorkin, Andres. *Int J Obes*, 1992;16:667-74.)

PROJECT NUMBER Z01 AG 07060 02 EDBP

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PERIOD COVERED

October 1, 1992 to September 30, 1993

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)

Biological Mediators of the Disease-Weight Loss Relation Among Older Persons in the Framingham Heart Study

PRINCIPLE INVESTIGATOR (List other professional personnel below the Principle Investigator.)

(Name, title, laboratory, and institute affiliation.)

Tamara Harris, M.D., M.S. Chief, Geriatric Epidemiology Office, EDBP, NIA
Ronald Prior, Ph.D., Scientific Program Officer, Human Nutrition Research Center on Aging
Irwin Rosenberg, M.D., Director, Human Nutrition Research Center on Aging at Tufts University

COOPERATING UNITS (if any)

USDA-Agricultural Research Service

LAB/BRANCH

Geriatric Epidemiology Office

SECTION

Epidemiology, Demography, and Biometry Program

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
	.05	

CHECK APPROPRIATE BOX(ES)

X (a) Human subjects X (b) Human tissues O (c) Neither

O (a1) Minors

O (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The purpose of this agreement is to fund the drawing, transporting, processing and analysis of blood specimens from the Framingham Heart Study cohort in Examination Cycle 22 and the collection of bioelectric impedance data from the members of the Framingham Heart Study cohort in Examination Cycle 22.

Data collection in Framingham is moving along well. The measurement of cytokine levels in mononuclear cells at Tufts, levels of inflammatory proteins and associated other biochemistries has been successful. Methodologic work over the year suggests that the delay of an hour in laboratory processing while the specimens are being transported has some effect on the measurements but that data from healthy younger persons in Framingham should allow some adjustment. Preliminary data on both stimulated and unstimulated levels of IL-1, TNF and IL-6 shows fairly normal distributions of secretors and non-secretors for each cytokine. Preliminary analyses are ongoing and data collection should be complete this fall.

Biometry Office

The Biometry Office conducts research in the mathematical, statistical and numerical aspects of aging and health. The Office is responsible for methodologies used in research programs related to aging and studies factors which affect health, disease and longevity. The Office performs a variety of functions involving the development and application of mathematical and statistical methods for EDB Program data on the epidemiology and demography of aging and health. The Office also provides statistical consulting, computing, graphics, and data management services to the other units within EDB as well as other Programs within the NIA, other NIH Institutes, other Government agencies, and the private sector.

The personnel of the Biometry Office has remained the same during Fiscal Year 1993, with Dr. Dwight Brock continuing to serve as Office Chief. Recruitment of a mathematical statistician to fill a position which has been vacant for 3 years was hampered by a hiring freeze last year and other reasons. For example, a potential candidate accepted an overseas assignment at the last minute. Since that time a considerable effort has gone into recruitment of new candidates. Several persons have been interviewed and an offer is pending review by Building 1. We hope to come to closure on this action soon.

The developmental activities and achievements of the Biometry Office are summarized below by project.

1. Established Populations for Epidemiologic Studies of the Elderly (EPESE)

Ms. Mary Lafferty continues to serve as Project Officer for the East Boston Senior Health Project (contractor, Brigham and Women's Hospital). She serves as data manager for the EDB Program, providing quality control of data management, editing and cleaning. Her data management responsibilities for the East Boston site coincide with her duties of project monitoring, resulting in improvements in the overall quality of the data. During the past year, staff for the East Boston project matched their cohort with Medicare Part A data provided by the Health Care Financing Administration (HCFA) for the years 1985 to 1990. It is expected that a no-cost modification to the final year of the contract will make it possible to match hospitalization data from HCFA for the years 1991 and 1992. In addition, the cohort data are being linked to the National Death Index for ongoing surveillance of vital status and successive cohort data are being cleaned. The contract was recently modified to include the microfiching of each questionnaire from baseline to the sixth followup year.

Mr. Daniel Foley continues to serve as Project Officer for the Yale Health and Aging Project (contractor, Yale University). A no-cost modification to the final year of the contract will provide 2 more years of hospitalization data from HCFA before the close of the contract. To date, all deliverables have been received on time and no cost overruns are anticipated for this final close-out year.

Dr. Brock continues to serve as Project Officer for the EPESE site at Duke University Medical Center. This site has had a very active year, having been in the field with the third in-person survey for most of the year. The interviewing has just been completed, but collection of blood samples from the participants is still under way, lagging the interviews by several weeks. It is expected that the last samples will be drawn early in the fall. As mentioned in last year's report, the timing of the interviews does not meet the expected one-year interval because of a 4-month delay in obtaining OMB clearance for this wave of interviewing. Although the Contractor met its requirement for submission of the OMB request, the various levels of clearance within the Public Health Service did not maintain the expected schedule. Thus, it will be necessary to make adjustments in the analyses of the third in-person survey data to account for unequal spacing of the interviews. This may require additional statistical methods development beyond what had been planned.

The investigators at Duke have been able to maintain very high response rates for the interviews during the current wave. Interview completion rates have exceeded 95 percent throughout this wave, and response to the blood draw has held between 75 percent and 80 percent. In addition to the standard protocols for analysis of blood samples done at the first three EPESE sites, the Duke site is including three measures of immune or clotting function, Interleukin-6 (IL-6), cross-linked fibrin degradation products (XDP fibrin D-dimers) and serum protein electrophoresis (SPE) measures of immune globulins. A study of intraindividual variability in these measures has been completed on 16 persons representing four race-sex groups. None of these persons is a regular Duke EPESE participant. For this study, eight plasma samples were obtained from each individual, separated by several days' time. Kappa statistics for IL-6 and XDP, assuming subjects are random and no difference due to day of measurement, gave values of 0.97 and 0.93, respectively. These high Kapppa values show that a single reading from an individual should be representative of all of that individual's measurements. Further, the variability <u>between</u> persons was sufficiently high that the data on the entire cohort should be very interesting to analyze. At the present time for the whole cohort 1,530 plasma samples have been collected, 1,045 have been analyzed for XDP, 950 for IL-6 and 700 for SPE. This work will continue into the fall, with a report and a data set to be submitted by the Contractor in January of next year.

Once the fieldwork for in-person III is completed, the Duke site will begin concentrated efforts on matching the cohort to the Medicare hospitalization files of HCFA and the National Death Index, as has been done in the other three EPESE sites. In addition, Duke will maintain surveillance of mortality and nursing home admissions through contacts with the cohort and other means used in the other sites. This work will continue for a period of 4 years.

With the lifting of the travel restrictions late in FY 1992, it was possible for Dr. Brock to make a site visit to the Duke EPESE project during an important period in its progress. A number of meetings and discussions took place with the Duke staff over a 2-day period near the end of September. Highlights of the visit included a discussion and resolution of a problem with recruiting and retaining qualified phlebotomists to conduct the blood drawing in

the field during the third in-person survey. In some cases it was necessary to hire emergency medical technicians (EMT's) to collect the blood samples. However, the problem was resolved, and as stated above, the project is now back on a reasonable schedule. There was an opportunity to observe a field interview being conducted with an EPESE participant. This was an invaluable experience for the observer, since there had been no previous opportunity to study the effectiveness of certain questionnaire and protocol items first hand. In particular, the physical performance measures (various types of stands, timed walk, etc.) had not been administered in previous waves of the study, and observation of the performance of these activities provided valuable insight as to the problems that older persons face with regard to functioning and activities of daily living. In addition, a number of potential data quality problems were observed and resolved on the spot, with note made to inform all the other interviewers of such difficulties. In all, the observation of the interview was an extremely valuable experience.

Other discussions at the visit included concerns regarding data editing, imputation, processing and analysis. A proposal was made for some statistical methodology work on two possible applications of the Grade-of-membership models developed by researchers at Duke for studying both cross-sectional and longitudinal data on physical functioning. A final discussion with the Principal Investigator covered the overall "health" of the project and plans for the additional work needed after the third in-person survey was completed.

Dr. Brock made a second visit to Duke in June of 1993 along with Ms. Lafferty, to meet with Duke staff and discuss in considerable detail all aspects of the data management, editing and processing operation. A number of data tape submissions were in need of corrections, and the communications established in these meetings have gone a long way toward finalizing the data sets for analysis and later archiving. In addition, progress reports were obtained in all aspects of the study, in particular the immunology substudy. Again, a one-day visit proved to be very valuable for both EDB staffers.

Ms. Caroline Phillips has served as alternate Project Officer for data linkage between HCFA MEDPAR 1985 through 1990 data and EPESE data for the three original sites (East Boston, Iowa, and New Haven). The pilot match (a minimum of 500 EPESE participants) for each site was completed by February 1992. Ms. Phillips reviewed results of the pilot match and contacted data management personnel at the sites with comments and questions. She gave a preliminary report of principal and secondary diagnoses from the Iowa HCFA data for years 1985-1990 at an EPESE PI's meeting; Iowa had completed a pilot match of all participants in the file, rather than the 500 people originally planned, so that there were enough data on which to report. Ms. Phillips initiated and coordinated a conference call with EPESE data management personnel and NIA staff to discuss requirements and schedule for the final HCFA match for years 1985-1990. At the time of the call, the sites agreed to have preliminary full match results completed by October 1992. Another conference call occurred approximately one month before the due date, to discuss any problems or issues. Ms. Phillips reviewed results of the preliminary full match with the sites in November 1992. The final files were due and were received in December 1992; however, since some additional

problems were uncovered in the December submission, the sites were allowed to resubmit a clean version of the file, which they did by February 1993.

Both the sites and NIA collaborated on the final file layout, which includes some variables in addition to those on the MEDPAR record. The revised format includes match codes, developed by the sites to indicate the certainty of the match; a year code indicates the year of HCFA data; a type of facility code indicates whether the participant was in a short stay hospital, long stay hospital, or skilled nursing facility. In addition, Ms. Phillips developed a series of five revised International Classification of Diseases (ICD)-9 diagnostic codes, which were appended to the end of the record. These revised codes were designed to help the researcher, in that the first digit of the code is always alphabetic (e.g., "E") or blank, and the numeric characters follow, with up to two decimal places.

Ms. Phillips developed documentation for the EPESE data linkage, incorporating documentation from HCFA, summaries of data linkage activities and descriptions of match codes written by data managers at the sites, and a brief history of the project. This documentation was completed in June 1993. It is believed that these data will be extremely valuable in providing the ability to study hospitalization end-points related to the vast array of health characteristics measured on the members of the EPESE cohorts. Several of those analyses are in early stages of development now.

Mr. Foley continues to develop findings from the EPESE on the topic of driving in late life. In the sixth EPESE followup, trained interviewers used standardized instruments to objectively measure physical functioning (Guralnik et al, submitted), distant visual acuity (Salive et al, 1992 in Ophthalmology), and mental status (Katzman, White, Losonczy, et al, accepted by J of Clinical Epidemiology). Linkage of these data to the driving data gathered in 1989 showed that physical frailty was not associated with an increase in crashes based on records maintained by the Divisions of Motor Vehicles in Connecticut (1988-1990) and Iowa (1987-1989). However, drivers in the New Haven cohort with distant visual acuity of 20/60 or worse were at a five-fold increase in risk for a crash involvement. The state of Connecticut requires drivers to renew licenses every 4 years whereas Iowa requires drivers age 70 and older to renew every other year. Our subjects were aged 70 or older when they were interviewed in 1988 (Foley et al, Submitted to AJPH for special issue on aging). No association was found between poor performance on the mental status questionnaire (MSQ) and an increased risk for crashes, although these results were limited by a small number of subjects failing the MSQ.

Also, investigators from Yale University in collaboration with Mr. Foley completed an analysis of data on risk factors for driving cessation (Marittoli, Ostfeld, Merrill, Perlman, Foley, and Cooney: J of Gerontology, in press). In summary, among the older drivers in the New Haven cohort, self-reported functional disability, neurologic diseases, history of cataracts, increasing age, lower income, and not working were risk factors for quitting.

Mr. Foley has collaborated with staff from the National Highway Traffic Safety Administration (NHTSA) to identify research resources which could address the relationship between dementia and driving. Currently Mr. Foley is discussing with NHTSA and staff from the Agency for Heath Care Policy and Research (AHCPR) the feasibility of linking crash records in the State of New York with records from the statewide Alzheimer's Disease Registry which has been in place since 1987. Also, under a grant award, investigators at the University of Iowa have received funds to recontact participants in the Iowa cohort for another round of interviews. Additional funds were provided by an interagency agreement with NHTSA to reassess driving practices. Mr. Foley has collaborated with investigators at Iowa regarding the analyses of these data.

Ms. Lafferty has prepared an EPESE baseline data file which has been archived at the National Archive of Computerized Data on Aging, Ann Arbor, Michigan, and at the National Archives, Washington, DC. The file included most of the baseline questionnaire items common to the three original EPESE sites but some of the data had to be modified to protect the confidentiality of the subjects. This file was submitted with documentation, tables, and file formats. Work is underway on the release of the second set of data which will include baseline data from the North Carolina site and questionnaire data from the first 3 years of followup at the three original sites. In addition, occurrences of death will be submitted with these data for the first 3 years of followup.

Biometry Office staff have continued to participate in a number of analyses of data from the EPESE during the past fiscal year.

Investigators at EDBP and Yale University have completed the linkage of data from the Connecticut Nursing Home Admissions Registry and are in the process of merging these data with the HCFA hospitalization data for analyses on the transfer of nursing home residents to hospitals. This analytic effort is led by Mr. Foley and Dr. Lisa Berkman at Yale University.

Mr. Foley has assumed the lead in the multi-site analyses of sleep complaints in collaboration with Dr. Monjan from the NNA program, who is the former Executive Chairman of the National Sleep Disorders Commission which issued its report in 1992. At baseline, over half of the EPESE participants reported a complaint relating to sleep and as many as 20 percent suffered from insomnia. The prevalence and incidence of chronic diseases and other medical conditions were found to be highly associated with sleep complaints. Work is in progress to develop statistical models for the chronic disease and chronic sleep complaints relationship. Dr. Brock is also collaborating in this analysis.

Three of the EPESE sites have received data on Medicare hospitalizations occurring between 1985 and 1990. Mr. Foley is collaborating with Dr. Tamara Harris and Ms. Phillips, along with other agency investigators on the subject of hospitalizations due to dehydration. Hospitalizations with dehydration either as a principal reason for admission or as a concomitant condition have risen dramatically over the past decade, according to analysis of trend data from the National Hospital Discharge Survey and the Medicare Hospitalization

data (Warren, Bacon, Harris, McBean, Foley and Phillips, Submitted to AJPH for special issue on aging). Hospitalization data from the EPESE reveal that over 450 subjects were hospitalized between 1985 and 1990 with dehydration and will be the basis for a risk factor study using the EPESE interview data.

Ms. Katalin Losonczy, in collaboration with Drs. Harris, Eleanor Simonsick, Joan Cornoni-Huntley and others has completed an analysis of EPESE data which examined the effects of baseline (age 70 years and older) weight, weight at age 50 and percent weight change on subsequent mortality. A final draft paper is underway. Data from all four sites were utilized in this work, which necessitated some adjustments in methodologic approaches taken in the analysis. Each weight variable was considered in sex-specific quintiles of body mass index (weight in kg/height in m^2) with the middle quintile as the reference group. Risk of death in old age was greatest for those who had been in the heaviest quintile of body mass index as age 50. However, this pattern reversed for body mass index at age 70 and older where the thinnest quintile had the greatest risk of death. Furthermore, those with weight loss of $\geq$ 10 percent showed an increased risk of mortality relative to those who remained weight stable, and were more likely to be ill or disabled. Exclusion of those who lost $\geq$ 10 percent of their weight and adjustment for additional health-related factors eliminated the risk of death associated with the thinnest quintile of body mass index at age 70 years and older. These results were presented at the annual meeting of the Society for Epidemiologic Research in Keystone, Colorado in June of 1993.

Ms. Losonczy is underway with two additional analyses of EPESE data. One analysis is examining EPESE drug data on the use of antioxidant supplements, aluminum and anticholinergics, and aspirin intake reported at baseline and followup III as possible correlates of cognitive impairment, and cancer and coronary heart disease mortality ascertained at followup VI. The second analysis looks at biochemical measures and weight change in the EPESE cohort. Both of these efforts will be continuing through FY 1993 and into FY 1994.

Drs. Brock and Jack Guralnik have been collaborating with a large group of EPESE investigators on an analysis of change in physical functioning, using baseline and 5 years of follow-up data for the four EPESE sites. Longitudinal methods were used to characterize the histories of physical function obtained, including rate of change and transitions into and recoveries from impairment. The average decline in physical function associated with age is greater than previous cross-sectional studies have suggested, and the rate of decline accelerates with increasing age. There is much individual variation, however, with many people experiencing declines and a smaller but substantial portion experiencing recovery. Women report a greater rate of decline in physical function and are less likely to recover from impairment. An invited papers session at the annual meeting of the American Public Health Association last November was devoted to the presentation of these analyses. Subsequently a written version of these results has been prepared and submitted for publication in the Milbank Quarterly.

Two other collaborative analyses of EPESE data are continuing. In the first, Dr. Brock is working with Dr. Jon Lemke of the University of Iowa and others on baseline correlates and predictors of hearing loss in the four EPESE populations. This is a rather complicated analysis due to the large number of factors that appear to influence self-reports of hearing loss and to variations in the associations among the sites. It is noteworthy that in New Haven and North Carolina, where a substantial portion of the cohorts are African-American, that the self reports indicate lower levels of loss among the racial minorities. However, when interviewer reports of hearing loss on the part of the respondents are taken into account, the prevalence of hearing loss appears to more nearly coincide with what has been observed in other studies such as the National Health and Nutrition Examination Survey. As a result of these findings, we are now proposing a second paper to examine the methodological issue in more detail.

The second analysis, led by Dr. Robert Glynn at East Boston, with collaboration from Drs. Havlik and Brock, has dealt with changes in blood pressure across the three in-person examinations in the first three EPESE sites. In East Boston and New Haven mean systolic blood pressure (SBP) decreased substantially over time, and the prevalence of elevated SBP decreased in each of five age cohorts and both sexes. Mean levels of SBP were lowest in Iowa where they increased slightly over time. Use of antihypertensives increased over time in all three populations, suggesting that some but not all of the observed blood pressure changes were explained by increases in the initiation of antihypertension therapy. This analysis has been accepted for presentation at the next annual meeting of the Gerontolgical Society of America in November of 1993.

2. National Health and Nutrition Examination Survey (NHANES), NHANES Epidemiologic Follow Study (NHEFS) and National Ambulatory Medical Care Survey (NAMCS) Analyses

Where appropriate, Biometry Office staff have continued to work with data from the national surveys operated by the National Center for Health Statistics (NCHS).

Ms. Losonczy and Dr. Lon White completed an analysis and submitted the results of an examination of the association of age-dependent disease and dietary vitamin E intake using data from the National Health and Nutrition Examination Survey, Cycle II (NHANES II). Applying logistic regression models, the authors found a significantly lower odds ratio for coronary heart disease in men and women, systolic hypertension and cataracts in women, and emphysema in men among those with the highest intake of dietary vitamin E compared to the lowest intake. Models were adjusted for other factors commonly associated with the diseases examined.

Dr. Marcel Salive, in collaboration with Drs. Guralnik and Brock, completed an analysis of data on preventive services for breast and cervical cancer in office-based practice from the National Ambulatory Medical Care Survey (NAMCS). The study was undertaken to

examine patterns of delivery of preventive services for breast and cervical cancer and the bundling of several preventive services. An estimated 38.7 million office visits included one or more preventive services for breast and cervical cancer, largely by obstetricians and gynecologists, with fewer such services having been provided by other specialties (e.g., general/family practice and general internal medicine). Only some 22 percent of these visits were periodic preventive visits, indicating that such visits have received only limited acceptance by physicians who provide preventive care for adult women.

Ms. Lafferty is the NIH coordinator for NHANES I and National Health Examination Follow-up Study (NHEFS) data. She makes corrections as required and disseminates information about these data to the NIH community. She and her staff oversee all data delivered to the Program and have computerized a listing of all files on tape. This provides a valuable resource to the entire NIH epidemiologic community, as these data are often the first source of information sought about numerous topics that are of interest to many NIH epidemiologists.

3. Survey of the Last Days of Life (SLDOL)

Data analysis has continued throughout FY 1993 for this study of death and dying in a community sample of older decedents in Fairfield County, Connecticut. A preliminary analysis of changes in residence due to episodes of health care use in the last 90 days of life was presented at the American Statistical Association meeting late in 1992. The analysis has been carried further since that time and current results are being prepared for submission to the special issue of American Journal of Public Health on aging. In brief, the study showed that transitions from the community to long-term care settings in the last days of life were associated with a clinical diagnosis of Alzheimer's disease, poor physical functioning, incontinence and the lack of family (spouse or children) to care for the individual at home. On the other hand, shorter stays and transitions to hospital settings were not as readily modeled by the variables available from the study, probably reflecting the fact that Medicare policies and sources of payment were more likely to influence such transitions. Final models have been fitted to these data and a manuscript is being prepared for submission for publication.

Another analysis from the SLDOL regarding the circumstances of death (Foley et al, in preparation for submission to The Gerontologist) showed that nearly 3/4 of deaths occur in a hospital or nursing home. Also, about 15 percent of deaths were classified as sudden deaths based on information abstracted from the death certificates. For the remaining decedents, about 10 percent of the surviving relatives reported that they were dissatisfied with the care received in the last months of life. We inferred from our descriptive summaries on the circumstances of death that more family discussion of the value of advance directives in late life including preference for medical care decision-making and use of life-support technology are warranted.

A third analysis from the SLDOL is being conducted by Ms. Losonczy in collaboration with Drs. Brock and White. In this study indices of physical and cognitive function have been constructed from a series of questions asked of the informant regarding the decedent's ability to recognize friends and family, to perform usual activities of daily living, and whether a physician had ever made a clinical diagnosis of Alzheimer's disease or any other dementia. The functioning questions were asked relative to three time periods during the last year of the decedent's life -- a typical day one year before death, a typical day one month before death, and the day before death. Using the responses to these questions, we examined factors associated with deterioration in both physical and cognitive function over the entire last year of life. Preliminary results showed that a diagnosis of dementia, poor physical functioning, incontinence and in some cases history of Parkinson's disease were associated with both cognitive and physical deterioration in the last year of life. On the other hand presence of cancer and coronary heart disease were associated with lower likelihood of a dementia diagnosis. The analyses of these data are continuing.

4. National Mortality Followback Survey (NMFS)

The EDBP is continuing to support through an interagency agreement the design, development and conduct of the 1993 National Mortality Followback Survey (NMFS). The survey will be used to investigate: (1) socioeconomic differentials in mortality, (2) potentials for prevention of premature death by inquiring into associations between risk factors and cause of death, (3) health care services provided in the last year of life, (4) disability, and (5) reliability of certain items reported on the death certificate. Data from next-of-kin informants, health care facilities and medical examiner/coroners will be combined with data from a nationally-representative sample of death certificates. In addition, identifying information will be collected to enable investigators to examine Medicare hospitalization records for the decedents in this study.

The specific purpose of the EDBP agreement is to fund an oversampling of 1,000 deaths of persons who die at age 100 or older to better understand cause of death, health care utilization in the last year of life, disability and the use of special equipment, and risk factors -- particularly level of physical activity -- among this segment of the population. There is evidence from the EPESE, for example, to suggest that stopping smoking, even at older ages, leads to better outcomes for older persons. The NMFS will enable EDBP to investigate such relationships at a national level. In addition, the inclusion of questions on cognitive function and clinical diagnosis of Alzheimer's disease will enable comparisons with the SLDOL and to establish trends between the 1986 and 1993/4 NMFS's. Linkage of this sample with HCFA hospitalization data will also allow study of possible compression of morbidity in very old decedents.

To date a pretest has been conducted in four states, establishing the feasibility of the types of questions to be investigated in the main survey and showing that high levels of response can be expected from the informants. Drs. Brock and Simonsick have been working with the

staff at NCHS to finalize the questions which pertain to our specific interests in this study. Upon completion of the analysis of the pretest data, final versions of the questionnaire will be prepared and the sampling of death certificates for the main study will begin. It is expected that the majority of the interviews will be conducted by telephone, as that mode was used successfully in the pretest and appeared to provide high quality data at substantially lower costs than face-to-face interviews. The interviewing will be done by Census Bureau interviewers, beginning in January of 1994. It is expected that data collection will continue for approximately one year, and that a final data tape will be available for analysis about one year after the data collection is completed.

5. Data Management/Computing/Graphics

The most important elements of the data quality management for the EDB Program continue to reside with the statistical computing/programming staff, directed by Ms. Lafferty. The staff continues to analyze EPESE data and design programs to check these data for completeness, accuracy and consistency. In addition, the staff was responsible for the preparation of file formats for each site and for each year. This work has been completed and includes final counts for each variable and for each site except for the last years of the North Carolina site at Duke University, which is still generating new data.

With the contracts for the first three EPESE sites in their final year, Ms. Phillips is working on the final review of each file with emphasis on the mortality and status files (which continue to be submitted as scheduled), on the HCFA data, and on the seventh followup (driving behavior). The fourth site (Duke) continues to provide new and corrected data every 6 months. The baseline interview file, and the files for the first 4 years of followup have been accepted by the staff, although many corrections remain to be made. Ms. Lafferty has worked closely with the computing support contractor, Tasqe, Inc., to update editing programs and to develop new programs as they are needed for this process. Ms. Josephine Cruz has integrated the Duke questionnaire into the common portion of file formats for the Fifth and Sixth Followups and prepared new formats for the Duke Supplements.

Ms. Lafferty serves on the data management committee for the Women's Health and Aging Study. The data for the First Fifty Cohort of this new study have been delivered and Ms. Phillips and Ms. Lafferty are reviewing the quality of these data. These data have been stored on our network server and the data will be analyzed using PC/SAS and other PC software. Over the next several months activity on this study will be increasing as more and more data become available for analysis. It is expected that computing staff responsibility in this area will increase concomitantly.

Upon Ms. Lafferty's recommendation, the Program has purchased eleven new 486 DX (with math co-processor) personal computers. Virtually the entire professional staff is now equipped with 486 computers. Plans are underway to upgrade the remaining 286 computers since most new software is written for 386 or newer computers and require more hard disk

capacity and random access memory (RAM) than is available on the older computers. Ms. Lafferty and Ms. Phillips have been working with the NIA Network Communications staff to ensure that the Program's special needs have been considered with the installation of a new faster and higher capacity file server and new network software. They have also assisted with the design of the system. With more speed and capacity we are now able to perform more data analysis without incurring the cost of mainframe computing.

Ms. Lafferty serves as liaison for the computing support services contractor, Tasqe, Inc. The contract has been continued for a third year, with many EDB staff utilizing the services of the contractor on a large variety of projects, from installation and evaluation of new software to management and analysis of data from many sources, to office automation.

Under the direction of Ms. Lafferty, Warren Wilbur, a summer student employee, has inventoried all the Program's PC's and peripherals, parts and other equipment in storage, and the software. He was also responsible for setting up most of the new equipment and software.

Ms. Cruz has continued to provide high quality graphics for most members of the EDBP staff and for other organizations both within and outside NIA. As most EDBP scientists prepare papers for presentation and publication as part of their regular duties, Ms. Cruz's contributions to the overall productivity of the Program remain a vital part of EDBP operations. In addition to her regular work in this area, Ms. Cruz has provided assistance with graphics requests from the Geriatrics Program, the Biology of Aging Program, the Office of Extramural Affairs, the Office of Planning, Analysis and International Activities and to a variety of guest researchers, visiting scientists and others. Finally, Ms. Cruz provides a valuable training function in working with both the summer students and the new stay-in-school employees to orient them into these methods of preparing computer graphics.

6. Statistical Methodology

The focus of activity in this area has been on further development and application of methods for analysis of longitudinal data. As mentioned earlier, Dr. Brock presented the results of modeling EPESE longitudinal data on physical functioning using random effects linear models at the most recent meeting of the American Public Health Association. In addition, he and Dr. Laurel Beckett, formerly with the East Boston EPESE site, prepared a poster paper on an evaluation of several methods for longitudinal analysis, which Dr. Brock presented at the NIH conference on current topics in biostatistics in January of 1993. This presentation included evaluation of not only the random effects models but also Markov models for studying transitions among states of disability and Cox proportional hazards models which treat the development of disability as a type of survival process.

Additional collaborative work with Dr. Beckett has been done this fiscal year on the extension of some of the longitudinal models to the complex sample survey setting. Complex

sample designs are being used increasingly for large-scale longitudinal studies in order to obtain accurate estimates in important subgroups and to study risk factors that are small to moderate in effect. Examples include the New Haven and Duke EPESE samples; the East Boston study on clinical evaluation of dementia, which selected a subsample of East Boston cohort members based on performance on a battery of cognitive function tests; the NCHS NHEFS and Longitudinal Study on Aging; and the Honolulu Dementia Study, which also subsampled in a manner similar to that used in East Boston. To date there has been little experience in adapting the increasingly sophisticated models proposed for discrete longitudinal data to the complex sample setting. In our work the Markov transition models for discrete longitudinal data, previously applied to simple random samples, have been examined, comparing three approaches for adjusting for the design to the unadjusted analysis: (1) unweighted regression including covariates for the design variables, (2) weighted logistic regression ignoring missing data, and (3) pseudo maximum likelihood estimation for the full Markov model. The results showed that using regression methods to adjust for design variables does not greatly affect parameter estimates if the regression model is carefully evaluated, although the standard error estimates are likely to be underestimated because of within-person clustering which is not accounted for by this method. The logistic method is likely to produce biased estimates of the parameters when there are numerous gaps in the longitudinal sequence of the data due to missing values. Further, using complete case analysis (using only those subjects with responses at all interviews) is likely to lead to substantial biases and cannot be recommended unless the amount of missing data is small. The full Markov model can provide useful estimates and appropriate standard errors, provided that the assumptions of memorylessness and stationarity of the process hold, both of which can be evaluated by residual analysis. The results of this study will be presented at the upcoming meeting of the American Statistical Association in August.

Further studies of the Markov model are planned in which the assumption of stationarity (that is, the risk factors and other covariates do not change over time) will be relaxed. This can readily be done using the logistic model, but considerable additional work will be required for the full Markov model using pseudo maximum likelihood, particularly in the area of software development. Other future topics of interest in this area include modeling mortality in these analyses as an absorbing state and relaxing the assumption of equally-spaced observations to model random sojourn times in each state of the system.

Drs. Beckett and Brock are currently negotiating with a publisher to produce a monograph which summarizes all the results of the evaluations of the various statistical models for analysis of longitudinal data.

Dr. Brock recently began discussions with Drs. Max Woodbury and Carl Pieper at Duke University regarding further development and applications of the Grade-of-membership (GOM) technique for analyzing longitudinal data. In the past, attempts to fit these models to our data have not been successful, primarily because of software problems. Dr. Woodbury has been working to provide software which is more user-friendly for testing by EDBP staff. He is also working toward the development of a short course designed to introduce

epidemiologists and others to the technique. Dr. Brock and Dr. Pieper have discussed a project in which GOM would be used to characterize physical functioning by creating so-called "pure types" of function (as provided by the GOM models) using all 14 questions available from the various waves of EPESE interviewing.

Dr. Brock has been requested on several occasions to provide sample size estimates for new studies (Women's Health and Aging Study and Health, Aging and Body Composition, e.g.) and occasionally for subsamples for existing studies (Honolulu Dementia Study, e.g.). In some cases a considerable amount of prior data is available for use in developing such estimates. In many cases the literature is incomplete with regard to how best to incorporate the additional auxiliary data. As a result, some investigations have been done to take all available factors into account in these calculations, and simple software written to implement the procedures.

As reported last year, a new software package for performing proportional hazards modeling with complex survey data has been received from the Research Triangle Institute. The testing phase for this program has been completed and the software is now available for use by EDBP analysts. This project was funded in part by an interagency agreement with NCHS to provide updated and new software for complex surveys. The program will allow incorporation of dependencies induced by the sample design into analysis of hazard models for data sets such as the New Haven and Duke EPESE studies and for the clinical data from the Honolulu Dementia Study, which subsampled subjects from the Honolulu cohort according to performance on a screening cognitive function test. The program will allow the data to be reweighted to represent the entire cohort and will adjust standard error estimates to account for clustering induced by the sample design. Finally, analysts will be able to make comparisons between analytic results obtained by assuming simple random sampling and those based on fully adjusted analyses.

In response to a question from the Acting Director of NIA, Drs. White and Brock prepared estimates of the lifetime risk of Alzheimer's Disease, using data from the NCHS, the Census Bureau and the East Boston clinical evaluation study. Since the common dementing illnesses are irreversible, another way to view the question is to estimate what proportion of today's population will have dementia by the time of death. A simple answer, which is probably a lower bound, is provided by data from the 1986 National Mortality Followback Survey, in which it was estimated that approximately 11 percent of decedents were reported to have been diagnosed with dementia. To take a closer look at this question, however, we applied a single decrement life table procedure to estimate the number of Americans expected to die at specific ages and then multiply those numbers by a fraction corresponding to the estimated prevalence of dementia among persons dying at that age. The following numbers and percents were calculated (1) from Census data on the number of Americans alive in 1986, (2) from life-expectancy and expected age-at-death figures from NCHS projected population survival curves (also for 1986), and (3) from the estimated curve for the age-specific prevalence of dementia from the East Boston study. Using the Census and expected survival data, we estimated the numbers and proportions of today's U.S. population likely to die at

specified ages -- for example, between the ages of 50 and 59, 60 and 69, and so on up to 85 and older. Then, using our best estimate of the age-specific prevalence of dementia, we estimated the number and percent of persons in each of these age-at-death groups who have or will develop dementia in their lifetimes.

The results of these calculations indicate that a total of 66,078,300 Americans alive today, or 27 percent of the total U.S. population either have or will develop dementia during their lifetimes. This represents an upper bound on the prevalence of dementia at death. At the present time we are considering alternative methods for deriving these estimates and will be obtaining additional data on incidence from the East Boston study. This is clearly an area of great interest to this Institute, and we will continue to pursue this line of work.

7. Consultation, Collaboration and Other Professional Activities

Biometry Office staff have provided service in a variety of consultative, collaborative and review activities during Fiscal Year 1993.

Mr. Foley presented data from Iowa and New Haven EPESE on the prevalence of functional impairments among older drivers and the association with motor vehicle crashes at The Second World Conference on Injury Control held May 20-23, 1993, in Atlanta, Georgia.

Ms. Losonczy served as Advisory Panel member for a project initiated by the American Water Works Association to examine the association of aluminum in drinking water and Alzheimer's disease. As part of that work, she participated in the Advisory Panel meeting in Seattle, Washington, June 1993.

Mr. Foley served as an expert consultant on the subject of older drivers in a one-day symposium attended by members of the research community and administrators representing license renewal agencies for the states of New York, Ohio, Pennsylvania, California and two Canadian provinces. This symposium was held June 29 in Pittsburgh during the annual meeting of the American Association of Motor Vehicle Administrators.

Mr. Foley and Dr. Robin Barr from the Behavioral Sciences Research program at NIA had a letter to the editor of The Journal of the American Geriatrics Society published in which they questioned the methods for calculating risk ratios for driving with dementia. The authors of the article conceded in a response to the letter that the published methods were flawed and revised the risk estimates in accordance with the Foley and Barr recommendations (JAGS, August 1993).

Dr. Brock served as an NIH in-house reviewer for two separate studies which were seeking OMB clearance for questionnaires and protocols. The first was the NCI Prostate, Lung, Colon and Ovarian (PLCO) cancer screening clinical trial, a multi-year, multi-million dollar project designed to test the effectiveness of screening for those specific cancers. Dr. Brock

had served as a reviewer of proposals for the contracts earlier and was asked to review the final protocols because of his familiarity with the study. The other study was an NICHD grant-funded survey of geneticists in private practice. Dr. Brock's review dealt with the survey design and sampling plan for this study.

Dr. Brock served on a Qualifications Review Board for recruitment of statisticians for the National Institute on Drug Abuse.

Dr. Brock also served as a sampling consultant to the Women's Health Initiative, advising Dr. Harlan's staff with regard to appropriate management of survey interviewers for a multi-site survey effort in this study. The experience of the multi-center EPESE project was heavily drawn upon in providing this consultation.

Dr. Brock continues to serve as the Council of Chapters Representative to the American Statistical Association from the Washington area chapter. He also continues to volunteer time as a board member of the Washington Statistical Society (WSS), and he works with the WSS Quantitative Literacy Group, which fosters the teaching of statistics in elementary and secondary schools in the Washington area.

8. Honors and Awards

Caroline Phillips received an On-the-spot award for her work on the design of the logo for the Women's Health and Aging Study in November 1992.

Research Highlights FY93

- Data from the NIA Survey of the Last Days of Life show that, on average, both men and women spend about 2 weeks in the hospital during the last 90 days of life. In addition, men can expect to spend an average of two weeks in a nursing home, compared to an average of about 4 weeks among women during these last days of life. A history of Alzheimer's disease is a strong predictor for spending time in nursing home and consequently less time in the community. The development of data which describe the use of health care services in the last year of life and the factors which influence the use of these services will assist planners and policy makers in shaping cost-effective strategies for meeting the needs of persons dying at advanced age. For example, women are more dependent on receipt of in-patient days of care than are men, primarily as a result of a greater likelihood of being widowed and living alone. One of the strongest predictors for women to remain in the community was the number of children they had to turn to for help and comfort in their last months of life. Thus, in addition to the forces of morbidity which may drive up the costs of care, there are the social dynamics which can have a strong influence on these costs as well. (Brock, Foley, Johnson. *Proc Am Stat Assoc*, 1993 in press.)

- Data were analyzed from household interviews of the 4 EPESE sites to estimate the prevalence of prescription and nonprescription medication use among community-living elderly and to examine sociodemographic and health factors related to medications use. Prescription drugs were used by 60-68% of women. Nonprescription drugs were used by 52-68% of men and 64-76% of women. Use of prescription medications generally increased with age although use of nonprescription drugs was not associated with age. Men and women who smoked or used alcohol in the preceding year frequently took medications. Those who reported more depressive symptoms, impairments in physical functioning, hospitalizations, and had poorer self-perceived health status were most likely to take medications. However, 10-29% of respondents with fair or poor self-perceived health took no prescription medications, and 3-13% took neither prescription nor nonprescription medications. While further research appears warranted into potential overmedication of elders, particularly those with many depressive symptoms, these data suggest that studies of potential underuse in elders with poor health are equally important. (Chrischilles, Foley, Wallace, Lemke, Semla, Hanlon, Glynn, Ostfeld, Guralnik. *J Gerontol* 1992;47:M137-M144.)

- Information on the extent of use of prescription and over-the-counter drugs was obtained from a probability sample of black (n=2,152) and white (n=1,821) community-resident elderly in the Piedmont area of North Carolina. Multivariate analysis of a health services use model explained 36 percent of the variation in prescription drug use and 6 percent of the variation in over-the-counter drug use. Health status and use of the medical care system were the strongest predictors of prescription drug use; demographic characteristics and self-assessed health were significant factors in use of over-the-counter drugs. Similar models explained prescription drug use for blacks and whites, but there were marked race differences in the over-the-counter drug models. The availability of public and private resources (Medicaid and Medigap insurance) were significant predictors of prescription drug use for black and white elderly, and of over-the-counter drug use for black elderly. (Fillenbaum GG, Hanlon JT, Corder EH, Ziqubu-Page T, Wall WH, Brock DB. Am J Public Health, 1993 in press.)

CONTRACT

Name and Number: Peter Bent Brigham Hospital (NO1-AG-0-2107)

Title: Established Populations for the Epidemiologic Studies of the Elderly (EPESE)

Date Contract Initiated: June 30, 1980

Current Annual Level: $347,419

Objectives: The purpose of this project is to conduct epidemiologic investigations in a community to develop new knowledge concerning the medical and social factors in health and diseases of the aged.

Methods Employed: The project includes cross-sectional and prospective studies in a carefully defined and accessible population using standard field and analytical techniques. Yearly surveillance of the population is included.

Significance to Biomedical Research: The population over age 65 has been steadily increasing both in relative and absolute numbers. With this increase has come an awareness of a variety of health and social problems which are creating problems for our social and physical environment. To provide new knowledge, it is important to study representative community-dwelling populations. Within obvious logistical constraints populations will be available to the NIA scientific community for specific studies.

Proposed Course: Continued surveillance during a 5-year period (1983-93) will be based on the use of the National Death Index for mortality and the Health Care Financing Administration's Medicare data for morbidity. While contract closeout will occur this calendar year, intensive research efforts will continue.

Major Findings: Mortality associated with handedness was examined in two ways. A simulation using national data suggests that lower mean age at death among left-handed persons, previously offered as evidence of higher mortality, can be explained exclusively by the age distribution of laterality. Second, empiric evidence from the East Boston EPESE study of 3,774 older adults demonstrates that left-handedness is not associated with mortality (relative odds=1.04% confidence interval=0.79%, 1.39) (ref. 1).

Publications

1. Salive ME, Guralnik JM, Glynn RJ. Left-handedness and mortality. *Am J Public Health* 1993;83:265-67.

CONTRACT

Name and Number: Yale University (NO1-AG-O-2105)

Title: Established Populations for Epidemiologic Studies of the Elderly (EPESE)

Date Contract Initiated: June 30, 1980

Current Annual Level: $359,749

Objectives: The purpose of this project is to conduct epidemiologic investigations in a community to develop new knowledge concerning the medical and social factors in health and diseases of the aged.

Methods Employed: The project includes cross-sectional and prospective studies in a carefully defined and accessible population using standard field and analytical techniques. Yearly surveillance of the population is included.

Significance to Biomedical Research: The population over age 65 has been steadily increasing both in relative and absolute numbers. With this increase has come an awareness of a variety of health and social problems which are creating problems for our social and physical environment. To provide new knowledge, it is important to study representative community-dwelling populations. Within obvious logistical constraints populations will be available to the NIA scientific community for specific studies.

Proposed Course: Continued surveillance during a 5-year period (1989-93) will be based on the use of the National Death Index and the Health Care Financing Administration's Medicare data for morbidity. While contract closeout will occur this calendar year, intensive research efforts will continue.

Major Findings: Of the 120 cohort members who sustained a hip fracture in the 6-year study period, 22 died within 6 months of the fracture. Among survivors there was a sustained decline in function at 6 weeks after the fracture with little improvement by 6 months. At baseline, 86% could dress independently versus 49% at 6 months; 90% could transfer independently versus 32% at 6 months; 75% could walk across a room independently versus 15% at 6 months; 63% could climb a flight of stairs versus 8% at 6 months; and 41% could walk one-half mile versus 6% at 6 months. Physical function and mental status were the only baseline factors significantly associated with physical function at 6 months after the fracture in bivariate analysis, while physical function and depression were associated in multivariate analysis (ref. 1).

The influence of selected psychosocial factors as predictors of stroke incidence were studied in this cohort. The main psychosocial factor of interest was depression. Marital status, social support, social networks, and religiousness were also assessed as potential antecedent

or mediating factors. The data were based on 2,812 individuals aged 65 years and over living in New Haven, Connecticut. The incidence of stroke was monitored from the baseline interview in 1982 until December 1988. Depression, measured by the Center for Epidemiologic Studies Depression Scale (CES-D), was measured at baseline as were other predictor variables. Univariate Cox regression analyses revealed that higher CES-D scores were predictive of greater stroke incidence ($p < 0.05$). More frequent attendance at religious services was associated with lower incidence ($p < 0.001$). CES-D scores were also correlated with many measures of sociodemographic, health, and physical function factors in our multivariate analysis ($p < 0.05$). When combined with other significant predictor variables such as age, sex, hypertension, diabetes, diabetes, physical function, and smoking, neither depression nor religious attendance retained its significance (ref. 2).

The survival of elderly patients hospitalized for acute myocardial infarction who have emotional support was compared with that of patients who lack such support, while controlling for severity of disease, comorbidity, and functional status. Of 194 patients, 76 (39%) died in the first 6 months after myocardial infarction. In multiple logistic regression analyses, lack of emotional support was significantly associated with 6-month mortality (odds ratio, 2.9; 95% CI, 1.2 to 6.9) after controlling for severity of myocardial infarction, comorbidity, risk factors such as smoking and hypertension, and sociodemographic factors. When emotional support was assessed before myocardial infarction, it was independently related to risk for death in the subsequent 6 months (ref. 3).

Physical function was assessed as a predictor of stroke incidence for the noninstitutionalized elderly subjects with no previous history of stroke. Incidence of stroke was monitored from the baseline interview in 1982 until December 1988 ($n=167$). Physical function was measured by the Katz scale of activities of daily living and a three-item scale measuring gross mobility function (Rosow scale). Both measures of impairment of function were independently associated with stroke incidence controlling for age, sex, diabetes, hypertension, and angina ($p<0.001$). Our findings suggest that in elderly persons, physical disability is a newly identified risk factor for stroke (ref. 4).

Mortality risk during early bereavement was examined in the New Haven sample of 1046 married elderly persons 65 years and over, followed from 1982 to 1988. Cox' regression models with time-dependent covariates were computed to estimate mortality risk, while controlling for pre-widowhood sociodemographic and health-related variables. Elderly young-old (65-74) and old-old men (≥ 75) showed slightly elevated age-adjusted relative risks (RR) during the first 6 months of widowhood ($RR=1.69$; 95% CI:0.86-3.31 and $RR=1.79$; 95% CI:0.44-7.28 respectively). These RRs increased slightly after adjustment for pre-widowhood control variables. The age-adjusted RR during early widowhood for young-old women was 2.87 (%CI: 0.81-2.42), which increased to 3.86 (95% CI:1.11-13.45) after adjustment for sociodemographic and health-related variables. This analysis stresses the usefulness of Cox' regression models with time-dependent covariates to calculate mortality risk for variable periods after onset of widowhood adjusted for pre-widowhood

characteristics. However, the power of the study was limited, resulting in mostly insignificant risk estimates and wide confidence intervals. (ref. 5).

Publications

1. Marottoli RA, Berkman LF, Cooney LMJr. Decline in physical function following hip fracture. J Am Geriatr Soc 1992;40:861-866.

2. Colantino A, Kasl SV, Ostfeld AM. Depressive symptoms and other psychosocial factors as predictors of stroke in the elderly. Am J Epidemiol 1992;136:884-894.

3. Berkman LF, Leo-Summers L, Horwitz RI. Emotional and survival after myocardial infarction: A prospective, population-based study of the elderly. Ann Intern Med 1992;117:1003-1009.

4. Colantino A, Kasl SV, Ostfeld AM. Level of function predicts first stroke in the elderly. Stroke 1992;23:1355-1357.

5. Mendes de Leon CF, Kasl SV, Jacobs S. Widowhood and mortality risk in a community sample of the elderly: A prospective study. J Clin Epidemiol 1993;46:519-527.

CONTRACT

Name and Number: Duke University Medical Center (N01-AG-1-2102)

Title: Established Populations for Epidemiologic Studies of the Elderly (EPESE)

Date Contract Initiated: January 1, 1991

Current Annual Level: $959,790

Objectives: The purpose of this project is to conduct epidemiologic investigations in a biracial elderly population, 65 years of age and older, selected from both urban and rural locations.

Methods Employed: Descriptive and analytical epidemiologic studies of existing problems and surveillance of newly developing problems all with an emphasis upon future intervention and prevention have been conducted. Investigators conducted cross-sectional and prospective studies as well as more detailed problem-related studies in a carefully defined and accessible population using standard field and analytical techniques.

Significance to Biomedical Research: The NIA began funding three population studies of the elderly to determine the influences of social, environmental, behavioral, and economic forces on the mortality, morbidity, and utilization of health services in the elderly. These studies, however, were not fully representative of the U.S. elderly; specifically, they did not include a significant proportion of blacks. It is well known that distributions of certain risk factors and diseases differ between U.S. blacks and other racial groups. Therefore, the purpose of the 1984 contract was to conduct epidemiologic investigations in an elderly population of which at least 50 percent is black in order to develop new knowledge concerning the medical and social factors in health and diseases of the aging black population. In addition, both black and white subgroups in the study exhibit an excellent distribution on indicators of socioeconomic status, and participants have been selected from both urban and rural locations.

Proposed Course: A new 7-year contract was awarded to Duke University Medical Center January 1, 1991, to conduct a third in-person survey wave and continue surveillance for major endpoints. In this wave, begun in May 1992, Duke is gathering information comparable to that obtained by the other EPESE sites as well as items which are important for the study of the health of older black persons and racial and urban/rural differences. Physical performance measures being taken include tests of balance, a timed walk, chair stands, a test of shoulder range of motion, and functional reach. Waist/hip ratio, height and weight, and vision are also being ascertained. Blood assays include complete blood count, automated serum chemistries, and HDL cholesterol.

The interviewing has just been completed for the third in-person survey, but collection of blood samples from the participants is still under way, lagging the interviews by several weeks. It is expected that the last samples will be drawn early in the fall. Interview completion rates have exceeded 95 percent throughout this wave, and response to the blood draw has held between 75 percent and 80 percent. In addition to the standard protocols for analysis of blood samples done at the first three EPESE sites, the Duke site is including three measures of immune function, Interleukin-6 (IL-6), cross-linked fibrin degradation products (XDP fibrin D-dimers) and serum protein electrophoresis (SPE) measures of immune globulins. At the present time for the whole cohort 1,530 plasma samples have been collected, 1,045 have been analyzed for XDP, 950 for IL-6 and 700 for SPE.

Once the fieldwork for in-person III is completed, the Duke site will begin concentrated efforts on matching the cohort to the Medicare hospitalization files of HCFA and the National Death Index, as has been done in the other three EPESE sites. In addition, Duke will maintain surveillance of mortality and nursing home admissions through contacts with the cohort and other means used in the other sites. This work will continue for a period of 4 years.

Major Findings: Hypertension in blacks, compared with whites, occurs at higher prevalence rates, is more severe, and carries a worse prognosis for cardiovascular morbidity and mortality. The authors examined the degree to which black/white differences in hypertension in the elderly are explained by demographic variables, income, health behavior (smoking, obesity), health service use, and comorbid diabetes. The study population consisted of subjects participating in the Duke EPESE, initiated in 1984. Cross-sectional data reported here were collected between January 1986 and July 1987. Subjects were aged 65 years or older and were not institutionalized. Blacks were oversampled. Of 5,223 eligible persons, 4,163 (80%) agreed to be interviewed; 16% of the study subjects were white men, 30% white women, 19% black man, and 35% black women. The mean age for all groups was approximately 73 years. Forty-four percent of white men, 52% of the white women, 50% of black men, and 66% of black women had hypertension. Eighty percent of hypertensives were receiving pharmacologic therapy. Older age, female sex, lower socioeconomic status, obesity, and diabetes mellitus were associated with hypertension. After adjusting for covariables, black race/ethnicity remained an independent risk factor for high blood pressure in the elderly, with an adjusted odds ratio of 1.30 (ref.1).

Epidemiologic surveys, experimental studies in animals, and clinical trials in young and middle-aged patients with hypertension indicate that dietary potassium lowers blood pressure. The mechanism of the antihypertensive effect is not well defined. Variations in serum potassium within the physiologic range may directly affect vascular smooth muscle tone. Potassium may also influence the regulation of blood pressure through effects on sodium handling, aldosterone secretion, the renin/angiotensin system, renal kallikrein, eicosanoids, and atrial natriuretic peptide. This study was undertaken to confirm the blood pressure-lowering effect of potassium in older patients and to determine the mechanism of the antihypertensive effect. Twenty-two patients ≥ 60 yr of age were admitted to a Clinical

Research Unit for 8 days after a 2-wk period free of antihypertensive medication. Patients were placed on an isocaloric diet containing 200 mmol/day of Na^+, 70 mmol/day of K^+, and 500 mg/day of Ca^{2+} and were treated in a randomized, double-blinded manner with either potassium chloride (120 mmol/day) or placebo. After 4 days, patients were crossed over to the alternate treatment. Systolic blood pressure decreased 8.6 mm Hg (95% confidence interval -14.6, -2.6), and diastolic blood pressure decreased 4.0 mm Hg (-6.9, -1.0) during potassium chloride supplementation. There was no significant change in blood pressure during treatment with placebo. Serum K^+ was 3.9 ± 0.1 mmol/L after 3 days of placebo and 4.3 ± 0.1 after 4 days of potassium chloride ($P < 0.0002$). Urinary sodium excretion averaged 192 ± 11 mmol/day after placebo and 221 ± 8 after potassium treatment ($P < 0.002$). Potassium treatment was not associated with changes in supine or captopril-stimulated PRA, GFR, atrial natriuretic peptide level, or urinary excretion of thromboxane B_2 or 6-keto-prostagiandin F_{1m}. It was concluded that potassium chloride lower blood pressure and increased sodium excretion in older patients with mild hypertension. The blood pressure effect may be due in part to potassium-induced natriuresis (ref. 2).

Information on prescription and over-the-counter drug use, demographic and health characteristics, and use of health services was obtained from a probability-based sample of black (n=2,152) and white (n=1,821) community-resident elderly in the Piedmont area of North Carolina. Descriptive statistics were calculated. Linear regression, in which sample weights and design effects were taken into account, was used for the final models. For prescription drug use, 37% and 32% of the variance was explained for whites, and blacks, respectively (6% and 5% for over-the-counter drugs). Health status and use of medical services were the strongest predictors of prescription drug use for both races (with Medigap insurance also important for white and Medicaid for blacks). Demographic characteristics and self-assessed health were significant factors in use of over-the-counter drugs. Race independently predicted use of both types of drugs, but explained only a small proportion of the variance. The study concluded that health status and use of health services are important in explaining prescription drug use. Over-the-counter drug use is difficult to explain (ref. 3).

The prevalence of people and sites with attachment loss, pocket depth, *Actinobacillus axtinomycetemcomitans*, *Prevotella intermedia*, and *Porphyromonas gingivalis* are described for a random sample of 366 black and 297 white community-dwelling adults, aged 65 or over, residing in 5 counties in North Carolina. In addition, relationships between sites harboring these microorganisms and loss of attachment (LA) and pocket depth (PD) are presented in a manner that considers the lack of independence of sites within each person. Pocket depths and recession were measured on all teeth by trained examiners during household visits. Immunofluorescent assays for *A. actinomycetemcomitans, P. intermedia*, and *P. gingivalis* were conducted on subgingival plaque samples obtained from the mesiobuccal aspect of the four first molar teeth using paper points. The prevalences of *A.actinomycetemcomitans*, *P. intermedia*, and *P. gingivalis* were greater in blacks than in whites. The most striking difference was seen for *P. gingivalis*, which was found in 38.8% of blacks and 9.4% of whites. Similar relationships were found when the percent of sites with these organisms were assessed. Blacks with *P. gingivalis* or *P. intermedia* had a higher

prevalence of sites with LA ≥ 7 mm as compared to blacks not infected with *P. gingivalis* or P. intermedia. The same was true for whites. Similar relationships between *P. gingivalis* or *P. intermedia* and PD ≥ 6 mm were found for both blacks and whites. However, the greater prevalence for blacks than whites for LA ≥ 7 mm or PD ≥ 6 mm when both were infected with *P. gingivalis* or *P. intermedia* were suggestive trends rather than significant. Finally, a logistic regression model for LA ≥ 7 mm showed that race was no longer a significant explanatory variable when *P. gingivalis, P. intermedia*, last visit to the dentist being more than 3 years ago, and tobacco use were already in the model. It is clear that destructive periodontal disease is the result of a complex relationship among subgingival microflora and non-bacterial factors. The interaction between the microbial flora and these other factors present a fruitful area of investigations in order to fully understand the complexity of periodontal disease in adults (ref. 4).

Publications

1. Svetkey LP, George LK, Burchett BM, Morgan PA, Blazer DG. Black/white differences in hypertension in the elderly: An epidemiologic analysis in central North Carolina. Am J Epidemiol 1993;137:64-73.

2. Smith SR, Klotman PE, Svetkey LP. Potassium chloride lowers blood pressure and causes natriuresis in older patients with hypertension. J Am Soc Nephrol 1992;2:1302-1309.

3. Fillenbaum GG, Hanlon JT, Corder EH, Zigubu-Page T, Wall WH, Brock D. Concomitants of prescription and over-the-counter drug use in black and white community resident elderly. Am J Public Health (in press).

4. Beck JD, Koch GG, Zambon JJ, Genco RJ, Tudor GE. Evaluation of oral bacteria as risk indicators for periodontitis in older adults. J Periodontol 1992;63:93-99.

PROJECT NUMBER Z01 AG 07030 05 EDBP

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PERIOD COVERED

October 1, 1992 to September 30, 1993

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)

NHANES III: Health of Older Person (Baseline Survey)

PRINCIPLE INVESTIGATOR (List other professional personnel below the Principle Investigator.)

(Name, title, laboratory, and institute affiliation.)

Richard J. Havlik, M.D., M.P.H., Associate Director, EDBP NIA
Kathy Lonsonczy, M.S., Biometry Office, EDBP, NIA
Robert Murphy, Division of Health Examination Statistics, NCHS

COOPERATING UNITS (if any)

National Center for Health Statistics

LAB/BRANCH

Biometry Office

SECTION

Epidemiology, Demography, and Biometry Program

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
	.05	

CHECK APPROPRIATE BOX(ES)

X (a) Human subjects O (b) Human tissues O (c) Neither

O (a1) Minors

X (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

NHANES III is a multi-agency collaborative survey designed to estimate the prevalence of diseases and risk factors in some 30,000 Americans and conducted by the National Center for Health Statistics. Special efforts are being directed to collection of data from interviews and examinations for the population over age 60 and the oldest-old.

Phase I of NHANES III, a national sample in itself and about one-half of the projected total, is completed. The overall examination rate is 78.7 percent and this rate is higher than for NHANES II. However, the response rates are somewhat lower for those 75 years and older. Home examinations are being done to improve the participation rate in older persons.

Biomedical examination content of particular interest to EDB Program investigators includes 24-hour dietary recalls, bioelectrical impedence for body composition, bone density measurement, knee x-rays, and an assessment of physical functioning. Phase I data files are becoming available for preliminary use. Phase II of NHANES III data collection is continuing at the same time and early participation rates have been high.

PROJECT NUMBER Z01 AG 07050 02 EDBP

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PERIOD COVERED

October 1, 1992 to September 30, 1993

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)

1993 National Mortality Followback Survey

PRINCIPLE INVESTIGATOR (List other professional personnel below the Principle Investigator.)

(Name, title, laboratory, and institute affiliation.)

Dwight B. Brock, Ph.D., Chief, Biometry Office, EDBP, NIA
Eleanor Simonsick, Ph.D., Epidemiology and Demography Office, EDBP, NIA
Paul Placek, Ph.D., Chief, Followback Survey, NCHS

COOPERATING UNITS (if any)

National Center for Health Statistics

LAB/BRANCH

Biometry Office

SECTION

Epidemiology, Demography, and Biometry Program

INSTITUTE AND LOCATION

NIA, NIH, Bethesda, MD 20892

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
	.08	

CHECK APPROPRIATE BOX(ES)

X (a) Human subjects O (b) Human tissues O (c) Neither

O (a1) Minors

X (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The purpose of this agreement is to support the collection and analysis of data on cause of death and characteristics of the last year of life in the planning of the 1992 Pretest and 1993 Main Survey of the 1993 National Mortality Followback Survey (NMFS), conducted by NCHS, CDC. This survey will supplement information from death certificates in the vital statistics file with information on characteristics of the decedent. The pretest will examine approximately 800 deaths of individuals aged 15 years and over who died in 1992. The main survey will examine approximately 20,000 deaths of individuals aged 15 years and over who died in 1993. This will include 1,000 deaths to centenarians.

A pretest has been conducted in four states, establishing the feasibility of the types of questions to be investigated in the main survey and showing that high levels of response can be expected from the informants. Upon completion of the analysis of the pretest data, final versions of the questionnaire will be prepared and the sampling of death certificates for the main study will begin. It is expected that the majority of the interviews will be conducted by telephone, as that mode was used successfully in the pretest and appeared to provide high quality data at substantially lower costs than face-to-face interviews. The interviewing will be done by Census Bureau interviewers, beginning in January of 1994. It is expected that data collection will continue for approximately one year, and that a final data tape will be available for analysis about one year after the data collection is completed.

National Institute on Aging
Epidemiology, Demography, and Biometry Program

PUBLICATIONS - FISCAL YEAR 1993

Andres R, Muller DC, Sorkin JD. Long-term effects of change in body weight on all-cause mortality. *Ann Intern Med* 1993;118 (in press).

Bachman DL, Wolf PA, Linn RT, Knoefek JE, Cobb JL, White LR, D'Agostino RB. Incidence of dementia and probable Alzheimer's disease in a general populatiion: The Framingham study. *Neurology* 1993;43:515-19.

Breslow RA, Sorkin JD. Comparison of one day and three day calorie counts in hospitalized patients: A pilot study. *J Am Geriatr Ass* 1993 (in press).

Brock DB, Foley DJ, Johson GR. Use of health care services in the last three months of life. *Proc Am Stat Assoc, Soc Stat Sect*, Washington, DC.:1992 274-79.

Campbell AJ, Busby WJ, Robertson MC, Lum CL, Langlois JA, Morgan FC. Disease, impairment, disability and social handicap: A community-based study of people 70 years and over. *Disability and Rehabilitation* 1993 (in press).

Cherry-Peppers G, Sorkin JD, Andres R, Baum BJ. Ship JA. Salivary gland function and glucose metabolic status. J Gerontol 1992; 47(4):M130-M134.

Chrischilles EA, Foley DJ, Wallace RB, Lemke JH, Semla TP, Hanlon JT, Glynn RJ, Ostfeld AM, Guralnik JM. Use of medications by persons 65 and over: Data from the established populations for epidemiologic studies of the elderly. *J Gerontol* 1992;47:M137-M144.

Cornoni-Huntley J, Ostfeld AM, Taylor JO, Wallace RB, Blazer D, Berkman LF, Evans DA, Kohout FJ, Lemke JH, Scherr PA, Korper SP. Established Populations for Epidemiologic Studies of the Elderly: Study design and methodology. *Aging Clin Exp Res* 1993;5:27-37.

Elias MF, Wolf PA, D'Agostino RB, Cobb J, White LR. Untreated blood pressure is inversely related to cognitive functioning: The Framingham study. *J Clin Epidemiol* 1993 (in press).

Fillenbaum GG, Hanlon JT, Corder EH, Zigubu-Page T, Wall WH, Brock DB. Concomitants of prescription and over-the-counter drug use in black and white community resident elderly. *Am J Public Health* 1993 (in press).

Ferrucci L, Bandinelli S, Guralnik JM, Lamponi M, Bertini C, Falchini M, Baroni A. Recovery of functional status after stroke: A post-rehabilitation follow-up study. *Stroke* 1993;24:200-05.

Ferrucci L, Guralnik J, Lamponi M, Costanzo S, Salani B, Marchionni N, Baroni A. Preclinical disability and performance measures of function. *Giorn Geront* 1992;40:227-33.

Guralnik JM, Land KC, Blazer D, Fillenbaum GG, Branch LG. Educational status and active life expectancy among older blacks and whites. *N Engl J Med 1993;329P:110-16.*

Guralnik JM, LaCroix AZ, Abbott RD, Berkman LF, Satterfield S, Evans DA, Wallace RB. Maintaining mobility in late life. I. Demographic characteristics and chronic conditions. *Am J Epidemiol* 1993;137:845-57.

Guralnik JM, Salive ME. Chronological and Functional Aging. In: Copeland JRM, Abou-Saleh MT, Blazer DG (editors). The Psychiatry of Old Age: An International Textbook. John Wiley and Sons, Sussex, U.K. 1993 (in press).

Guralnik JM, Simonsick EM. Physical disability in older americans. *J Gerontol* 1993 (in press).

Harris TB, Ballard-Barbasch R, Madans J, Makuc DM, Feldman JJ. Overweight, weight loss, and risk of coronary disease in older women: NHANES I Epidemiologic Followup Study. *Am J Epidemiol* 1993 (in press).

Harris TB, Burt V, Briefel RR, McDowell M, Sorenson A. The National Health and Nutrition Examination Survey III: Describing the health and nutritional status of older americans. *Aging Clinical and Experimental Research* 1993 (in press).

Ho SC, Bacon WE, Harris T, Looker A, Maggi S. Hip fracture rates in Hong Kong and the United States, 1988 through 1989. *Am J Public Health* 1993;83:694-97.

Ho SC, Harris TB, Madans J, Feldman JJ. Body mass index, mortality and disability among non-smoking elderly women: A comparative study between Hong-Kong and the United States. *Age & Nutrition* 1993;4:88-93.

Hoskins WJ, Yancik R, Trimble E. Conference summary: Recommendations for research. *Cancer* 1993;71(supp):655-58.

Kant AK, Glover C, Horm J, Schatzkin A, Harris TB. Does cancer survival differ for older patients? *Cancer* 1992;70:2734-70.

Kant AK, Schatzkin A, Harris TB, Ziegel RG, Block G. Dietary diversity and subsequent mortality in the first National Health and Nutrition examination survey Epidemiologic follow-up study. *Am J Clin Nutr* 1993;57:434-40.

LaCroix AZ, Guralnik JM, Berkman LF, Wallace RB, Satterfield S. Maintaining mobility in late life. II. Smoking, alcohol consumption, physical activity, and body mass index. *Am J Epidemiol* 1993;137:858-69.

Monfardini S, Yancik R. Cancer in the elderly: Meeting the challenge of an aging population. *J Natl Cancer Inst* 1993;85:532-38.

Ness RB, Harris TB, Cobb J, Flegal KM, Kelsey JL, Balanger A, Stunkard AJ, D'Agostino RB. Number of pregnancies and the subsequent risk of cardiovascular disease morbidity. *N Engl J Med* 1993 (in press).

Rumpel C, Harris TB, Madans J. Modification of the relationship between the Quetelet index and mortality by weight-loss history among older women. *Ann Epidemiol* 1993;3:343-50.

Salive ME, Guralnik JM, Christen W, Glynn RJ, Colsher P, Ostfeld AM. Functional blindness and visual impairment in older adults from three communities. *Ophthalmology* 1992;99:1840-47.

Salive ME, Guralnik JM, Glynn RJ. Left-handedness and mortality. *Am J Public Health* 1993;83:265-67.

Salive ME, Havlik RJ. Blood pressure and serum creatinine. *J Am Med Ass* 1993;269:2983-4 (letter).

Salive ME. Maxcy-Rosenau-Last Public Health and Preventive Medicine, 13th edition. *Military Medicine* 1992;157(11):A6 (book review).

Salive ME, Satterfield S, Ostfeld AM, Wallace RB, Havlik RJ. Disability and cognitive impairment are risk factors for pneumonia-related mortality in older adults. *Public Health Rep* 1993;108:314-22.

Salive ME, Wallace RB, Ostfeld AM, Satterfield S, Havlik RJ. Risk factors for septicemia-associated mortality. *Public Health Rep* 1993;108 (in press).

Seidell JC, Muller DC, Sorkin JD, Andres R. Fasting respiratory exchange ratio and resting metabolic rate as predictors of weight gain: The Baltimore Longitudinal Study on Aging. J Obesity 1992;16:667-672.

Simonsick EM. Relationship between husband's health status and the mental health of older women. J Aging Health 1993 (in press).

Simonsick EM, Lafferty ME, Phillips CL, Mendes de Leon CF, Kasl SV, Seeman TE, Fillenbaum G, Hebert JH. Risk due to inactivity in physically capable older adults. *Am J Public Health* 1993 (in press).

Teng EL, Hasegawa K, Homma A, Imai Y, Larson E, Sasaki H, White LR. A practical test for cross-cultural epidemiological studies of dementia: The cognitive abilities screening instrument (CASI). In: *New Horizons in Aging Science*, ed by H Orimo, Y Fukuchi, M Iriki. Univ of Tokyo Press, 1992.

Teng EL, Hasegawa K, Homma A, Imai Y, Larson E, Sugimoto K, Yamaguchi T, Sasaki H, Chiu D, White LR. The cognitive abilities screening instrument (CASI): A practical test for cross-cultural epidemiological studies of dementia. International Psychogeriatrics 1993 (in press).

White LR. Towards a program of cross-cultural research on the epidemiology of Alzheimer's disease. *Current Science* (India) 1992;63:456-69.

White LR. The Ni-Hon-Sea Dementia Project: Description and progress report. In: *New Horizons in Aging Scince*, ed by Orlmo H, Fukuchi K, Kuramoto K, Iriki M. Univ of Tokyo Press, 1992.

White L, Katzman R, Losonczy K, Salive M, Wallace R, Berkman L, Taylor J, Fillenbaum G, Havlik R. Association of education with incidence of cognitive impairment in three established populations for epidemiologic studies of the elderly. *J Clin Epidemiol* 1993 (in press).

Yancik R. Ovarian cancer: Age contrasts in incidence, histology, disease stage at diagnosis, and mortality. *Cancer* 1993;71:517-523.

Yancik R, Moore TD, Martin G, Obrams GI, Reed E. Older women as the focus for research and treatment of ovarian cancer: An overview for the National Institute on Aging, National Cancer Institute, and American Cancer Society Multidisciplinary Working Conference. *Cancer* 1993;71(supp):513-516.

National Institute on Aging

Epidemiology, Demography, and Biometry Program

September 1993

Associate Director
Richard J. Havlik, M.D., M.P.H.

Assistant Director, OD, NIA
Rosemary Yancik, Ph.D.

Assistant to Associate Director
Paulette Campbell

Secretary to Associate Director
Paula Williams

Clerk-Typist (summer)
Lisa Smith

Clerk-Typists (SIS)
Armilda Quispe
Binh Huynh

Epidemiology and Demography Office

Chief
Jack M. Guralnik, M.D., Ph.D.

Demographer
(Vacancy)

Epidemiologist
Marcel E. Salive, M.D., M.P.H.

Epidemiologist
Eleanor M. Simonsick, Ph.D.

Epidemiology Fellow
Lori Brown, Ph.D., M.P.H.

Visiting Fellow
Chiara Corti, M.D., M.H.S.

Guest Researchers
Marco Pahor, M.D.
Antonio Sgadari, M.D.

Epidemiologist (Temporary)
David Stein, M.D., M.P.H.

Asia-Pacific Office (Hawaii)

Chief
Lon R. White, M.D., M.P.H.

Study Team

NCNR Nurse
Carolyn Murdaugh, Ph.D.

VA Neurologist
G. Webster Ross, M.D.

VA Secretary
Stephanie Tecson

Geriatric Epidemiology Office

Chief
Tamara Harris, M.D., M.S.

Epidemiologist
Jean A. Langlois, Ph.D.

Epidemiologist
(New position/Expert)

Geriatrician*
Marian A. Parrott, M.D.

Epidemiology Fellow
John Sorkin, M.D.

Guest Researcher
Lenore J. Launer, Ph.D.

*Intergovernmental Personnel Act (IPA) Appointment

Biometry Office

Chief
Dwight B. Brock, Ph.D.

Statistician
Daniel J. Foley, M.S.

Data Manager
Mary E. Lafferty

Statistician
(Vacancy)

Statistician
Katalin G. Losonczy, M.A.

Computer Programmer Analyst
Caroline L. Phillips, M.S.

Computer Programmer
Josephine V. Cruz

Computer Assistant (summer)
Warren Wilbur

Z01 AG 07030 05
NHANES III: Health of Older Person (Baseline Survey)
Havlik, RJ

NHANES III is a multi-agency collaborative survey designed to estimate the prevalence of diseases and risk factors in some 30,000 Americans and conducted by the National Center for Health Statistics. Special efforts are being directed to collection of data from interviews and examinations for the population over age 60 and the oldest-old. Phase I of NHANES III, a national sample in itself and about one-half of the projected total, is completed. The overall examination rate is 78.7 percent and this rate is higher than for NHANES II. However, the response rates are somewhat lower for those 75 years and older. Home examinations are being done to improve the participation rate in older persons. Biomedical examination content of particular interest to EDB Program investigators includes 24-hour dietary recalls, bioelectrical impedence for body composition, bone density measurement, knee x-rays, and an assessment of physical functioning. Phase I data files are becoming available for preliminary use. Phase II of NHANES III data collection is continuing at the same time and early participation rates have been high.

Z01 AG 07040 03
Honolulu Aging Study
White, LR

The NIA supplements a research project sponsored by the NHLBI and supported through an NHLBI contract with Kuakini Medical Center in Honolulu, Hawaii, to allow for research on aging and dementia among study participants. The Honolulu Heart Program (HHP) is a prospective study of cardiovascular diseases of American men of Japanese ancestry born from 1900 to 1919 and living on the island of Oahu in 1965. This study will focus on aging, with the emphasis on Alzheimer's disease and multi-infarct dementia. About 3,800 of the approximately 4,600 HHP participants have been contacted thus far, including approximately 3,500 who have received all or almost all of the standard examination and interview. Approximately 20 to 25 minutes of the NHLBI examination is devoted to NIA data collection, including administration of the Cognitive Abilities and Screening Instrument (CASI) and a questionnaire to elicit information concerning possible risk factors for dementia. Approximately 13% of the examined participants were invited back for a follow-up examination. Those invited back include all of the participants who receive low CASI scores, about 33% of those who received borderline scores (74-82, N=176), and 7% of those who received normal (>82, N=165) CASI scores. The purpose of this call-back examination is to carry out a highly standardized dementia evaluation following guidelines previously agreed upon and from which an algorithmic dementia classification can be accomplished with a minimum of subjective interpretation and clinical judgement.

Z01 AG 07050 02
1993 National Mortality Followback Survey
Brock, DB

The purpose of this agreement is to support the collection and analysis of data on cause of death and characteristics of the last year of life in the planning of the 1992 Pretest and 1993 Main Survey of the 1993 National Mortality Followback Survey (NMFS), conducted by NCHS, CDC. This survey will supplement information from death certificates in the vital statistics file with information on characteristics of the decedent. The pretest will examine approximately 800 deaths of individuals aged 15 years and over who died in 1992. The main survey will examine approximately 20,000 deaths of individuals aged 15 years and over who died in 1993. This will include 1,000 deaths to centenarians.
A pretest has been conducted in four states, establishing the feasibility of the types of questions to be investigated in the main survey and showing that high levels of response can be expected from the informants. Upon completion of the analysis of the pretest data, final versions of the questionnaire will be prepared and the sampling of death certificates for the main study will begin. It is expected that the majority of the interviews will be conducted by telephone, as that mode was used successfully in the pretest and appeared to provide high quality data at substantially lower costs than face-to-face interviews. The interviewing will be done by Census Bureau interviewers, beginning in January of 1994. It is expected that data collection will continue for approximately one year, and that a final data tape will be available for analysis about one year after the data collection is completed.

Z01 AG 07060 02
Biological Mediators of the Disease-Weight Loss Relation Among Older Persons in the Framingham Heart Study
Harris, T

The purpose of this agreement is to fund the drawing, transporting, processing and analysis of blood specimens from the Framingham Heart Study cohort in Examination Cycle 22 and the collection of bioelectric impedance data from the members of the Framingham Heart Study cohort in Examination Cycle 22.

Data collection in Framingham is moving along well. The measurement of cytokine levels in mononuclear cells at Tufts, levels of inflammatory proteins and associated other biochemistries has been successful. Methodologic work over the year suggests that the delay of an hour in laboratory processing while the specimens are being transported has some effect on the measurements but that data from healthy younger persons in Framingham should allow some adjustment. Preliminary data on both stimulated and unstimulated levels of IL-1, TNF and IL-6 shows fairly normal distributions of secretors and non-secretors for each cytokine. Preliminary analyses are ongoing and data collection should be complete this fall.

Z01 AG 07070 01
Epidemiologic Studies on Brain Aging in Japan and the United States
White, LR

The Ni-Hon-Sea-Tai project is a coordinated series of epidemiologic studies on dementia that include a survey in the Adult Health Study Cohort of the Radiation Effects Research Foundation (REFR) in Hiroshima. The project was organized by the Asia-Pacific Office and is continued as a shared effort by cooperating scientists in Seattle, Kawasaki City, Taipei, Hiroshima, and Honolulu. A central goal is to develop and use methods sufficiently alike so that comparisons of rates and patterns of dementing illnesses across sites would be possible.

Coordination with the Hiroshima study was facilitated by establishment of an interagency agreement with the Department of Energy, through which funds were made available to the RERF for work related to our collaborative studies on dementia. A large part of these funds were used to support the participation of Japanese scientists in the Sixth Japan-U.S. Workshop on Methods for Cross-National Dementia Research.

The project is progressing well and it is likely that parallel studies using comparable methodologies will be conducted at two sites in the U.S., one or two sites in Japan, and at least two sites in Taiwan.

NIH Library, Building 10
National Institutes of Health
Bethesda, Md. 20892

7510005824201

LIBRARY
NIH
Amazing Research.
Amazing Help.
http://nihlibrary.nih.gov

10 Center Drive
Bethesda, MD 20892-1150
301-496-1080

NIH LIBRARY
3 1496 00497 5150